#### Research on the Safety of Vaping Devices and E-Cigarettes

The below list is continually growing but is by no means exhaustive. Apologies to those whose studies I've yet to include - Jay Pieski

Resource/Report

Date

Author

Key points

E-cigarettes around 95% less harmful than tobacco

Aug 2015 Public Health England

Key findings of the review include:

- · the current best estimate is that e-cigarettes are around 95% less harmful than smoking
- nearly half the population (44.8%) don't realise e-cigarettes are much less harmful than smoking
- there is no evidence so far that e-cigarettes are acting as a route into smoking for children or non-smokers

Web link: https://www.gov.uk/government/news/e-cigarettes-around-95-less-harmful-than-tobacco-estimates-landmark-review

Nicotine and toxicant yield ratings of ecigarettes in NZ

Med Journal)

Mar 2015 Laugesen (NZ "E-cigarettes available in New Zealand in 2013 exposed users to higher levels of nicotine than in older brands but lower than cigarettes, and to far lower levels of toxicants than cigarettes and earlier e-cigarettes, indicating potential as safer substitutes for tobacco."

Web link (PDF): https://www.scimex.org/ data/assets/file/0019/22906/E-cigs NZMJ.pdf

Electronic cigarette use Mar 2015 R Polosa and harm reversal: emerging evidence in the lung (commentary)

(BMC Medicine)

- · "In the only clinical study conducted to ascertain efficacy and safety of EC (electronic cigarette) use in asthma, substantial improvements in respiratory physiology and subjective asthma outcomes have been reported. Exposure to e-vapor in this vulnerable population did not trigger any asthma attacks.
- · The reported improvements of respiratory patients who have become regular ECs users are consistent with findings from a large internet survey of regular EC users diagnosed with asthma and COPD (chronic obstructive pulmonary disease). An improvement in symptoms of asthma and COPD after switching was reported in 65.4% and 75.7% of the respondents, respectively.
- Taken together, these findings provide emerging evidence that EC use can reverse harm from tobacco smoking."

Web link: http://www.biomedcentral.com/1741-7015/13/54 & http://tobaccoanalysis.blogspot.ca/2015/03/new-commentary-arquesthat-electronic.html?m=1

Comparison of ecigarettes, tobacco cigarettes and ambient air

Feb 2015 Regulatory Toxicology

and

Pharmacology: Tayyarah et al

The e-cigarettes contained and delivered mostly glycerin/glycol and water.

- Aerosol nicotine content was 85% lower than the cigarette smoke nicotine.
- The levels of harmful and potentially harmful constituents (HPHCs) in aerosol were consistent with the air blanks.
- Mainstream cigarette smoke HPHCs were 1500 times higher than ecigarette HPHCs.
- No significant contribution of tested HPHC classes was found for the e-cigarettes.
- Declared interests: The company for which the study authors work and the companies that manufacture the e-cigarettes tested for this study are owned by the same parent company.

'Keep calm it's only poison': Poison reports in context

Jan 2015 The counterfactual: Clive Bates

- Much has been made of the rapid rise in (ecigarette related) calls to US Poison Centers in recent years.
- But they make up a tiny fraction of all calls.
- It is also questionable how dangerous nicotine liquids actually are.
- But rather than panic, there is a simple measure, which meets the requirement for a duty of care to consumers. Just ensure tamper proof containers are used. Something the industry can easily do and increasingly does.

Web link: http://www.clivebates.com/?p=2740

Formaldehyde debate

Jan 2015 Multiple

See: formaldehyde tab.

Review: Are e-cigarettes Dec 2014 HCP Live:

a good thing?

"This review begins to tell us, mostly from observational and survey data, that EC's are less likely to induce nicotine dependence, less likely to be carcinogenic, and may help those who are trying to quit traditional cigarettes. Overall, this appears to be good news."

Web link: http://www.hcplive.com/publications/family-practice-recertification/2014/November2014/Are-E-Cigarettes-a-Good-Thing

Comparative in Vitro **Toxicology Profile:** ECigs, Tobacco Cigs, Smokeless Tobacco &

Nov 2014 Env Res & Pub Health: Misra et al

"The present findings indicate that neither the e-cig liquids and collected aerosols, nor the extracts of the Smokeless Tobacco and NRT products produce any meaningful toxic effects in four widely-applied in vitro test system."

NRT

Web link: http://www.mdpi.com/1660-4601/11/11/11325 & http://acsh.org/2014/11/yet-another-study-shows-absence-e-cigarettetoxins/

Action on Smoking and Nov 2014 ASH UK Health (ASH) briefing on e-cigarettes

"E-cigarettes are proving more attractive to smokers than NRT (i.e patches, gum) while providing them with a safer alternative to cigarettes. In the absence of evidence of significant harm to bystanders, ASH does not support the inclusion of electronic cigarettes in smokefree laws which would completely prohibit their use in enclosed public places."

Web link (pdf): http://ash.org.uk/files/documents/ASH 715.pdf

Blue e-Cig funded research comparing own product

Nov 2014 Regulatory

Toxicology

"Thus e-cigarettes are considerably less harmful than smoking tobacco, and switching from smoking tobacco to using electronic cigarettes appears to

and

have a positive impact on smokers' health."

with Marlboro cigarettes

Pharmacology:

Yan & Ruiz

Web link: http://www.sciencedirect.com/science/article/pii/S0273230014002797

Comparison of E-Cigarettes with Exhaled

Smoke from a Cigarette

Oct 2014 Long (Int. J. Environ. Res.

Public Health)

"Results indicate that exhaled e-cigarette aerosol does not increase

bystander exposure for phenolics and carbonyls above the levels observed

in exhaled breaths of air."

Web link: http://www.mdpi.com/1660-4601/11/11/11177

Vaping Report

Oct 2014 BBC's Trust

Me I'm a

Doctor

Small scale test for carbon monoxide associated with heart disease.

and acrolein associated with cancer and lung problems

The vapers had significantly lower levels similar to those found in non-

smokers

Web link: https://www.youtube.com/watch?v=nkiaSW8ZR1g&noredirect=1

Electronic cigarettes: fact and faction

Sep 2014 British Journal "Some reviews have bizarrely concluded that we do not know whether ecigarette use is safer than smoking, ignoring the fact that the vapour contains

of General Practice: West nothing like the concentrations of carcinogens and toxins as cigarette smoke. & Brown

In fact, toxin concentrations are almost all well below 1/20th that of cigarette smoke."

Web link: http://bjgp.org/content/64/626/442#ref-6

Particulate metals and organic compounds, second hand exposure

Aug 2014 Environmental Science:

Saffari et al

"Overall, with the exception of Ni, Zn, and Aq, the consumption of ecigarettes resulted in a remarkable decrease in secondhand exposure to all metals and organic compounds... Further analysis indicated that the contribution of e-liquid to the emission of these metals is rather minimal, implying that they likely originate from other components of the e-cigarette device or other indoor sources."

Web link: http://pubs.rsc.org/en/content/articlelanding/2014/em/c4em00415a#ldivAbstract

Analysis of poisoning reports

Mar 2014 Huff Post

Science:

"We also need to ask ourselves why we don't talk about other exposures

with the same sense of alarm.

Fairchild and Bayer

The convenience of clean laundry is a bigger threat than accidental exposure

to the liquid nicotine in e-cigarettes."

Web link: http://www.huffingtonpost.com/dr-amy-fairchild/liquid-death-from-ecigare\_b\_5044145.html

Report of nicotine liquid Jun 2014 Letter to New poisoning in small infant

Medicine: Bassett et al

10 month boy treated for ingesting vaping liquid with 1.8% nicotine Engl Journal of concentration (considered high strength) and wintergreen flavouring. Text padded with (outdated) assertion that a teaspoon of vaping liquid could kill an adult, finally returning to the subject to report that the "patient's levels of consciousness, hemoglobin oxygen, and serum salicylate, as well as findings on chest radiography and his basic metabolic profile, were all normal. The boy did not require antidote therapy and recovered baseline health in 6 hours".

Web link: http://www.nejm.org/doi/full/10.1056/NEJMc1403843

Review of studies of health benefits in switching from smoking to vaping

Spring 14 Journal of

Patient-Centered

Research and Reviews:

Brown et al

"In tobacco smokers unwilling to quit, switching to e-cigarettes:

- 1. decreases exhaled carbon monoxide level
- 2. decreases number of tobacco cigarettes smoked
- 3. reduces carcinogenic nitrosamine exposure levels compared to tobacco cigarettes
- 4. helps reduce smoking-related negative health effects"

More studies are needed, however "these early studies shed exciting new information on an addiction that has defied traditional treatment approaches."

Web link (pdf): http://www.aurorahealthcare.org/content/userfiles/files/JPCRR\_Volume1\_Issue2.pdf#page=35

Levels of toxicants much lower than cigarette smoke

Mar 2013 Goneiwicz et

al

"The levels of the toxicants were 9-450 times lower than in cigarette smoke and were, in many cases, comparable with trace amounts found in the reference product."

Web link: http://tobaccocontrol.bmj.com/content/early/2013/03/05/tobaccocontrol-2012-050859.short

Cytotoxicity evaluation May 2013 Romagna et al "EC vapor is significantly less cytotoxic compared to tobacco cigarette smoke"

Web link: http://informahealthcare.com/doi/abs/10.3109/08958378.2013.793439

Nicotine far less toxic than generally accepted Nov 2013 Houezec et al. Amzer

Glas, Rennes

"People smoke for nicotine, but other compounds may play a role in addictiveness.

There are no concerns of nicotine overdosing in e-cigarette users. Nicotine lethal dose has been overestimated. Regulators should take it into

The health risks from pure nicotine in humans appear to be small if any. Pure nicotine use, as with e-cigarettes, seems less addictive than when smoked in tobacco, and is considerably less harmful."

Web link (pdf): http://ecigarettereviewed.com/wp-content/uploads/2013/11/Nicotine-safety-in-the-context-of-e-cigarette-use-and-

E-cigarettes don't stiffen arteries

2013 Farsalinos et

al. Onassis

"Research on ECs should be intensified since they may be potentially useful in reducing the adverse vascular effects associated with smoking."

Cardiac

Surgery Center

Web link (pdf): http://www.ecigarette-research.com/EUROECHO2013-ecigs.pdf

Myocardial function study

Aug 2013 Farsalinos et al "Cardiac function: diastolic function acutely impaired in smokers, no

difference observed in experienced eCig users"

Web link (pdf): http://spo.escardio.org/eslides/view.aspx?eevtid=54&fp=1375

Metals in Electronic Cigarette Vapor

University

Apr 2013 Siegel, Boston "The total daily intake of these metals from the electronic cigarette brand tested by Williams et al. is far below the USP standard for each of the

School of

metals.

Public Health However, control measures need to be in place to minimize the presence of

metals in electronic cigarette aerosol."

Web link: http://tobaccoanalysis.blogspot.co.uk/2013/04/metals-in-electronic-cigarette-vapor.html

Chemistry analysis of e- Aug 2013 Burstyn,

Drexel Uni. USA

"By the standards of occupational hygiene, current data do not indicate that exposures to vapers from contaminants in electronic cigarettes warrant a

concern."

Web link (pdf): http://publichealth.drexel.edu/~/media/Files/publichealth/ms08.ashx

Higher nicotine content Jun 2013 Farsalinos et

al

A 20 mg/mL nicotine concentration liquid is needed to match one tobacco cigarette

needed help match tobacco delivery

cigarette vapours

Web link: http://www.mdpi.com/1660-4601/10/6/2500

Nicotine risks of 1st gen Sep 2012 Queen Mary devices

Uni London

"There is little risk that electronic cigarettes (EC) deliver toxic levels of

nicotine" (page 5)

Web link (pdf): http://www.mhra.gov.uk/home/groups/comms-ic/documents/websiteresources/con286844.pdf

Air quality study

Oct 2012 McAuley et al

"The study indicates no apparent risk to human health from e-cigarette

emissions based on the compounds analyzed."

Web link: http://www.ncbi.nlm.nih.gov/pubmed/23033998

**Public Health** Physicians and

Standards

aerosol

**Tobacco Researchers** 

Expose FDA's Double

2010

Siegel et al

"The FDA cited the detectable presence of carcinogens and 'toxic chemicals' in a 'small sample' of electronic cigarette cartridges as reason for alarm. singling out nitrosamines as particularly toxic. What the FDA fails to inform the public is that detectable amounts of carcinogens are also present in nicotine replacement products such as NicoDerm CQ and Nicorette gum, both approved by the FDA, and nitrosamines that can be also found in food

items such bacon and beer."

Web link: http://www.standardnewswire.com/news/162574365.html

Safety Report on the Ruyan® e-cigarette cartridge and inhaled

Oct 2008 Health NZ Ltd

"Ruyan® e-cigarette is designed to be a safe alternative to smoking. The various test results confirm this is the case. It is very safe relative to cigarettes, and also safe in absolute terms on all measurements we have applied."

Web link (pdf): http://www.healthnz.co.nz/RuyanCartridgeReport30-Oct-08.pdf

Long-term effects of inhaled nicotine

1996

Waldum et al

Rats given inhaled nicotine at twice the blood plasma level of a heavy

smoker for two years

"We could not find any increase in mortality, in atherosclerosis or frequency of tumors in these rats compared with controls.

Our study does not indicate any harmful effect of nicotine when given in its pure form by inhalation."

Web link: http://www.ncbi.nlm.nih.gov/pubmed/8614291

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E-cigarettes: an evidence update A report commissioned by Public Health England Authors: McNeill A, Brose LS, Calder R, Hitchman SC Institute of Psychiatry, Psychology & Neuroscience, National Addiction Centre, King's College London UK Centre for Tobacco & Alcohol Studies Hajek P, McRobbie H (Chapters 9 and 10) Wolfson Institute of Preventive Medicine, Barts and The London School of Medicine and Dentistry Queen Mary, University of London UK Centre for Tobacco & Alcohol Studies

#### **Executive Summary**

Following two previous reports produced for Public Health England (PHE) on ecigarettes (EC) in 2014, this report updates and expands on the evidence of the implications of EC for public health. It covers the EC policy framework, the prevalence of EC use, knowledge and attitudes towards EC, impact of EC use on smoking behaviour, as well as examining recent safety issues and nicotine content, emissions and delivery. Two literature reviews were carried out to update the evidence base since the 2014 reports and recent survey data from England were assessed. EC use battery power to heat an element to disperse a solution of propylene glycol or glycerine, water, flavouring and usually nicotine, resulting in an aerosol that can be inhaled by the user (commonly termed vapour). EC do not contain tobacco, do not create smoke and do not rely on combustion. There is substantial heterogeneity between different types of EC on the market (such as cigalikes and tank models). Acknowledging that the evidence base on overall and relative risks of EC in comparison with smoking was still developing, experts recently identified them as having around 4% of the relative harm of cigarettes overall (including social harm) and 5% of the harm to users. In England, EC first appeared on the market within the last 10 years and around 5% of the population report currently using them, the vast majority of these smokers or recent ex-smokers. Whilst there is some experimentation among never smokers, regular use among never smokers is rare. Cigarette smoking among youth and adults has continued to decline and there is no current evidence in England that EC are renormalising smoking or increasing smoking uptake. Instead, the evidence reviewed in this report point in the direction of an association between greater uptake of EC and reduced smoking, with emerging evidence that EC can be effective cessation and reduction aids. Regulations have changed little in England since the previous PHE reports with EC being currently governed by general product safety regulations which do not require products to be tested before being put on the market. However, advertising of EC is now governed by a voluntary agreement and measures are being introduced to protect children from accessing EC from retailers. Manufacturers can apply for a medicinal licence through the Medicines and Healthcare products Regulatory Agency (MHRA) and from 2016, any EC not licensed by the MHRA will be governed by the revised European Union Tobacco Products Directive (TPD).

https://www.gov.uk/government/uploads/system/uploads/attachment\_data/file/457102/Ecigarettes an evidence update A report commissioned by Public Health England FINAL.pdf

Electronic cigarette use and harm reversal: emerging evidence in the lung Riccardo Polosa

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UOC di Medicina Interna e d'Urgenza, Edificio 4, Piano 3, AOU "Policlinico-V. Emanuele", Via S. Sofia 78, Catania, 95123, Italy BMC Medicine 2015, 13:54 doi:10.1186/s12916-015-0298-3 The electronic version of this article is the complete one and can be found online

at:http://www.biomedcentral.com/1741-7015/13/54

#### **Abstract**

Electronic cigarettes (ECs) have been rapidly gaining ground on conventional cigarettes due to their efficiency in ceasing or reducing tobacco consumption, competitive prices, and the perception of them being a much less harmful smoking alternative. Direct confirmation that long-term EC use leads to reductions in smoking-related diseases is not available and it will take a few decades before the tobacco harm reduction potential of this products is firmly established. Nonetheless, it is feasible to detect early changes in airway function and respiratory symptoms in smokers switching to e-vapor. Acute investigations do not appear to support negative respiratory health outcomes in EC users and initial findings from long-term studies are supportive of a beneficial effect of EC use in relation to respiratory outcomes. The emerging evidence that EC use can reverse harm from tobacco smoking should be taken into consideration by regulatory authorities seeking to adopt proportional measures for the e-vapor category.

http://www.biomedcentral.com/1741-7015/13/54

#### Regulatory Toxicology and Pharmacology Volume 70, Issue 3, December 2014, Pages 704–710

Comparison of select analytes in aerosol from e-cigarettes with smoke from conventional cigarettes and with ambient air Rana Tayyarah, , Gerald A. Long

#### **Highlights**

The e-cigarettes contained and delivered mostly glycerin and/or PG and water.

Aerosol nicotine content was 85% lower than the cigarette smoke nicotine.

The levels of HPHCs in aerosol were consistent with the air blanks (<2 µg/puff).

Mainstream cigarette smoke HPHCs (  $3000 \ \mu g/puff$ ) were 1500 times higher than ecigarette HPHCs.

No significant contribution of tested HPHC classes was found for the e-cigarettes.

#### Abstract

Leading commercial electronic cigarettes were tested to determine bulk composition. The e-cigarettes and conventional cigarettes were evaluated using machine-puffing to compare nicotine delivery and relative yields of chemical constituents. The e-liquids tested were found to contain humectants, glycerin and/or propylene glycol, ( 75% content); water (<20%); nicotine (approximately 2%); and flavor (<10%). The aerosol collected mass (ACM) of the e-cigarette samples was similar in composition to the eliquids. Aerosol nicotine for the e-cigarette samples was 85% lower than nicotine yield for the conventional cigarettes. Analysis of the smoke from conventional cigarettes showed that the mainstream cigarette smoke delivered approximately 1500 times more harmful and potentially harmful constituents (HPHCs) tested when compared to ecigarette aerosol or to puffing room air. The deliveries of HPHCs tested for these ecigarette products were similar to the study air blanks rather than to deliveries from conventional cigarettes; no significant contribution of cigarette smoke HPHCs from any of the compound classes tested was found for the e-cigarettes. Thus, the results of this study support previous researchers' discussion of e-cigarette products' potential for reduced exposure compared to cigarette smoke.

http://www.sciencedirect.com/science/article/pii/S0273230014002505

Addiction. 2014 Nov;109(11):1801-10. doi: 10.1111/add.12659. Epub 2014 Jul 31. Electronic cigarettes: review of use, content, safety, effects on smokers and potential for harm and benefit.

<u>Hajek P1, Etter JF, Benowitz N, Eissenberg T, McRobbie H.</u>
<u>Author information</u>

#### **Abstract**

#### AIMS:

We reviewed available research on the use, content and safety of electronic cigarettes (EC), and on their effects on users, to assess their potential for harm or benefit and to extract evidence that can guide future policy.

#### **METHODS:**

Studies were identified by systematic database searches and screening references to February 2014.

#### **RESULTS:**

EC aerosol can contain some of the toxicants present in tobacco smoke, but at levels which are much lower. Long-term health effects of EC use are unknown but compared with cigarettes, EC are likely to be much less, if at all, harmful to users or bystanders. EC are increasingly popular among smokers, but to date there is no evidence of regular use by never-smokers or by non-smoking children. EC enable some users to reduce or quit smoking.

#### CONCLUSIONS:

Allowing EC to compete with cigarettes in the market-place might decrease smoking-related morbidity and mortality. Regulating EC as strictly as cigarettes, or even more strictly as some regulators propose, is not warranted on current evidence. Health professionals may consider advising smokers unable or unwilling to quit through other routes to switch to EC as a safer alternative to smoking and a possible pathway to complete cessation of nicotine use.

 $\frac{\text{http://www.ncbi.nlm.nih.gov/pubmed/?term=Electronic+cigarettes\%3A+review+of+use\%}{2C+content\%2C+safety\%2C+effects+on+smokers+and+potential+for+harm+and+benef}{\underline{it}}$ 

Int. J. Environ. Res. Public Health 2014, 11(11), 11325-11347; doi:10.3390/ijerph111111325

Article

Comparative In Vitro Toxicity Profile of Electronic and Tobacco Cigarettes, Smokeless Tobacco and Nicotine Replacement Therapy Products: E-Liquids, Extracts and Collected Aerosols

<u>Manoj Misra</u> \* , <u>Robert D. Leverette</u>, <u>Bethany T. Cooper</u>, <u>Melanee B. Bennett</u> and <u>Steven E. Brown</u>

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(This article belongs to the Special Issue <u>Electronic Cigarettes as a Tool in Tobacco</u> Harm Reduction)

View Full-Text | Download PDF [683 KB, 4 November 2014; original version 30 October 2014] | Browse Figures

#### Abstract

The use of electronic cigarettes (e-cigs) continues to increase worldwide in parallel with accumulating information on their potential toxicity and safety. In this study, an in vitro battery of established assays was used to examine the cytotoxicity, mutagenicity, genotoxicity and inflammatory responses of certain commercial e-cigs and compared to tobacco burning cigarettes, smokeless tobacco (SLT) products and a nicotine replacement therapy (NRT) product. The toxicity evaluation was performed on e-liquids and pad-collected aerosols of e-cigs, pad-collected smoke condensates of tobacco cigarettes and extracts of SLT and NRT products. In all assays, exposures with e-cig liquids and collected aerosols, at the doses tested, showed no significant activity when compared to tobacco burning cigarettes. Results for the e-cigs, with and without nicotine in two evaluated flavor variants, were very similar in all assays, indicating that the presence of nicotine and flavors, at the levels tested, did not induce any cytotoxic, genotoxic or inflammatory effects. The present findings indicate that neither the e-cig liquids and collected aerosols, nor the extracts of the SLT and NRT products produce any meaningful toxic effects in four widely-appliedin vitro test systems, in which the conventional cigarette smoke preparations, at comparable exposures, are markedly cytotoxic and genotoxic.

http://www.mdpi.com/1660-4601/11/11/11325

# Regulatory Toxicology and Pharmacology Volume 71, Issue 1, February 2015, Pages 24–34

Effects of using electronic cigarettes on nicotine delivery and cardiovascular function in comparison with regular cigarettes

X. Sherwin Yan, , Carl D'Ruiz

#### Highlights

E-cig users showed significantly lower nicotine C90 than Marlboro® cigarette users.

Use of Marlboro® cigs led to significant elevation of blood pressure and heart rate.

Use of e-cigs showed less magnitude of increase of BP and HR than cigarette smoking.

Use of Marlboro® cigs significantly increased the exhaled CO 8+ times above baseline.

#### **Abstract**

The development of electronic cigarettes (e-cigs) has the potential to offer a less harmful alternative for tobacco users. This clinical study was designed to characterize ecig users' exposure to nicotine, and to investigate the acute effects of e-cigs on the hemodynamic measurements (blood pressure and heart rate) in comparison with the effects of regular smoking. Five e-cigs and one Marlboro® cigarette were randomized for twenty-three participants under two exposure scenarios from Day 1 to Day 11: half-hour controlled administration and one hour ad lib use. The nicotine plasma concentrations after 1.5 h of product use (C90) were significantly lower in the users of e-cigs than of Marlboro® cigarettes. The combination of glycerin and propylene glycol as the vehicle facilitated delivery of more nicotine than glycerin alone. The heart rate, systolic and diastolic blood pressure were significantly elevated after use of Marlboro® cigarettes, but the elevation was less after use of most of the e-cigs. Use of e-cigs had no impact on the exhaled CO levels, whereas the Marlboro® cigarette significantly increased the exhaled CO more than 8 times above the baseline. In conclusion, e-cigs could be a less harmful alternative for tobacco users.

http://www.sciencedirect.com/science/article/pii/S0273230014002797

Comparison of Select Analytes in Exhaled Aerosol from E-Cigarettes with Exhaled Smoke from a Conventional Cigarette and Exhaled Breaths Gerald A. Long

Lorillard Tobacco Company, P.O. Box 21688, Greensboro, NC 27420, USA

Received: 21 August 2014 / Revised: 14 October 2014 / Accepted: 16 October 2014 /

Published: 27 October 2014

(This article belongs to the Special Issue Electronic Cigarettes as a Tool in Tobacco

Harm Reduction)

View Full-Text | Download PDF [519 KB, uploaded 27 October 2014] | Browse

**Figures** 

#### **Abstract**

Exhaled aerosols were collected following the use of two leading U.S. commercial electronic cigarettes (e-cigarettes) and a conventional cigarette by human subjects and analyzed for phenolics, carbonyls, water, glycerin and nicotine using a vacuum-assisted filter pad capture system. Exhaled breath blanks were determined for each subject prior to each product use and aerosol collection session. Distribution and mass balance of exhaled e-cigarette aerosol composition was greater than 99.9% water and glycerin, and a small amount (<0.06%) of nicotine. Total phenolic content in exhaled e-cigarette aerosol was not distinguishable from exhaled breath blanks, while total phenolics in exhaled cigarette smoke were significantly greater than in exhaled e-cigarette aerosol and exhaled breaths, averaging 66 µg/session (range 36 to 117 µg/session). The total carbonyls in exhaled e-cigarette aerosols were also not distinguishable from exhaled breaths or room air blanks. Total carbonyls in exhaled cigarette smoke was significantly greater than in exhaled e-cigarette aerosols, exhaled breath and room air blanks, averaging 242 µg/session (range 136 to 352 µg/session). These results indicate that exhaled e-cigarette aerosol does not increase bystander exposure for phenolics and carbonyls above the levels observed in exhaled breaths of air.

http://www.mdpi.com/1660-4601/11/11/1177

Particulate metals and organic compounds from electronic and tobacco-containing cigarettes: comparison of emission rates and secondhand exposure

<u>Arian Saffari,a Nancy Daher,a Ario Ruprecht,b Cinzia De Marco,c Paolo Pozzi,c Roberto Boffi,c Samera H. Hamad,d Martin M. Shafer,d James J. Schauer,d Dane Westerdahle and Constantinos Sioutas\*a</u>

#### **Show Affiliations**

Environ. Sci.: Processes Impacts, 2014,16, 2259-2267

DOI: 10.1039/C4EM00415A

Received 27 Jul 2014, Accepted 21 Aug 2014 First published online 22 Aug 2014

#### Abstract

In recent years, electronic cigarettes have gained increasing popularity as alternatives to normal (tobacco-containing) cigarettes. In the present study, particles generated by ecigarettes and normal cigarettes have been analyzed and the degree of exposure to different chemical agents and their emission rates were quantified. Despite the 10-fold decrease in the total exposure to particulate elements in e-cigarettes compared to normal cigarettes, specific metals (e.g. Ni and Ag) still displayed a higher emission rate from e-cigarettes. Further analysis indicated that the contribution of e-liquid to the emission of these metals is rather minimal, implying that they likely originate from other components of the e-cigarette device or other indoor sources. Organic species had lower emission rates during e-cigarette consumption compared to normal cigarettes. Of particular note was the non-detectable emission of polycyclic aromatic hydrocarbons (PAHs) from e-cigarettes, while substantial emission of these species was observed from normal cigarettes. Overall, with the exception of Ni, Zn, and Ag, the consumption of e-cigarettes resulted in a remarkable decrease in secondhand exposure to all metals and organic compounds. Implementing quality control protocols on the manufacture of e-cigarettes would further minimize the emission of metals from these devices and improve their safety and associated health effects.

http://pubs.rsc.org/en/content/articlelanding/2014/em/c4em00415a#!divAbstract

CORRESPONDENCE
Nicotine Poisoning in an Infant

N Engl J Med 2014; 370:2249-2250 June 5, 2014

DOI: 10.1056/NEJMc140384

#### To the Editor:

Reports to U.S. poison control centers of possible nicotine toxicity tripled from 2012 to 2013.1.2Although nicotine toxicity is not a new phenomenon, the emergence of electronic cigarettes ("e-cigarettes") has spawned a market for highly concentrated liquid nicotine. This phenomenon has resulted in unprecedented access to potentially toxic doses of nicotine and other harmful compounds in the home. We report a case of a child who was poisoned by e-cigarette refill liquid ("e-liquid").

Vomiting, tachycardia, grunting respirations, and truncal ataxia developed in a 10-month-old boy after he ingested a "small" amount of e-liquid nicotine. The vaping (or "vape") shop that compounded the product reported that it contained a nicotine concentration of 1.8% (18 mg per milliliter) and unknown concentrations of oil of

wintergreen (methyl salicylate), glycerin, and propylene glycol.

Multiple toxidromes that could have been associated with ingestion of this type of product include cholinergic crisis and salicylism. Low doses of nicotine frequently have stimulant effects (e.g., tachycardia). Vomiting is common with enteral exposures. Signs of central nervous system toxicity include ataxia and seizures. As doses increase, loss of nicotinic receptor specificity may occur and result in signs of muscarinic cholinergic toxicity, including extreme secretions and gastrointestinal disturbance. The highest levels of poisoning can result in neuromuscular blockade, respiratory failure, and death. Small ingestions could be deadly. With an estimated median lethal dose between 1 and 13 mg per kilogram of body weight, 1 teaspoon (5 ml) of a 1.8% nicotine solution could be lethal to a 90-kg person.3,4

Fortunately, our patient's levels of consciousness, hemoglobin oxygen, and serum salicylate, as well as findings on chest radiography and his basic metabolic profile, were all normal. The boy did not require antidote therapy (usually atropine or scopolamine to combat cholinergic activity) and recovered baseline health 6 hours after ingesting the

poison.

The Food and Drug Administration does not currently regulate nontherapeutic nicotine; this raises concern that in the ballooning unregulated liquid nicotine market there may be variability in nicotine dosing and introduction of unintended toxic ingredients. Lack of regulatory oversight has resulted in inconsistent labeling, insufficient or nonexistent child protective packaging, and product design and flavoring that may encourage children to explore and ingest these products. Figure 1

FIGURE 1

Three Examples of Over-the-Counter Liquid Nicotine Products. shows labeling that contains suggestions of edible ingredients ("lemonade"), visually appealing cartoons, and handwritten labels of uncertain reliability. With the growing use of e-cigarettes, physicians need to be alert for nicotine poisoning. They also need to educate patients and parents about this danger and advocate for

measures that will help prevent potentially fatal liquid nicotine poisoning of infants and young children.

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Kevin Osterhoudt, M.D.Children's Hospital of Philadelphia, Philadelphia, PA Tecla Brabazon, D.O.Abington Health Lansdale Hospital, Lansdale, PA <u>Disclosure forms</u> provided by the authors are available with the full text of this letter at NEJM.org.

This letter was published on May 7, 2014, at NEJM.org.

http://www.nejm.org/doi/full/10.1056/NEJMc1403843#t=article

Tob Control doi:10.1136/tobaccocontrol-2012-050859
Research paper
Levels of selected carcinogens and toxicants in vapour from electronic cigarettes

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Received 24 October 2012 Accepted 31 January 2013 Published Online First 6 March 2013

#### **Abstract**

Significance Electronic cigarettes, also known as e-cigarettes, are devices designed to imitate regular cigarettes and deliver nicotine via inhalation without combusting tobacco. They are purported to deliver nicotine without other toxicants and to be a safer alternative to regular cigarettes. However, little toxicity testing has been performed to evaluate the chemical nature of vapour generated from e-cigarettes. The aim of this study was to screen e-cigarette vapours for content of four groups of potentially toxic and carcinogenic compounds: carbonyls, volatile organic compounds, nitrosamines and heavy metals.

Materials and methods Vapours were generated from 12 brands of e-cigarettes and the reference product, the medicinal nicotine inhaler, in controlled conditions using a modified smoking machine. The selected toxic compounds were extracted from vapours into a solid or liquid phase and analysed with chromatographic and spectroscopy methods.

Results We found that the e-cigarette vapours contained some toxic substances. The levels of the toxicants were 9–450 times lower than in cigarette smoke and were, in many cases, comparable with trace amounts found in the reference product.

Conclusions Our findings are consistent with the idea that substituting tobacco cigarettes with e-cigarettes may substantially reduce exposure to selected tobacco-specific toxicants. E-cigarettes as a harm reduction strategy among smokers unwilling to quit, warrants further study. (To view this abstract in Polish and German, please see the supplementary files online.)

http://tobaccocontrol.bmj.com/content/early/2013/03/05/tobaccocontrol-2012-050859.short

Inhalation Toxicology: International Forum for Respiratory Research Volume 25, Issue 6, 2013

#### Research Article

Cytotoxicity evaluation of electronic cigarette vapor extract on cultured mammalian fibroblasts (ClearStream-LIFE): comparison with tobacco cigarette smoke extract

DOI:10.3109/08958378.2013.793439

Giorgio Romagnaa, Elena Allifranchinia, Elena Bocchiettoa, Stefano Todeschia, Mara

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pages 354-361

Publishing models and article dates explained

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#### Abstract

Context: Electronic cigarettes (ECs) are used as alternatives to smoking; however, data on their cytotoxic potential are scarce.

Objective: To evaluate the cytotoxic potential of 21 EC liquids compared to the effects of

cigarette smoke (CS).

Methods: Cytotoxicity was evaluated according to UNI EN ISO 10993-5 standard. By activating an EC device, 200 mg of liquid was evaporated and was extracted in 20 ml of culture medium. CS extract from one cigarette was also produced. The extracts, undiluted (100%) and in five dilutions (50%, 25%, 12.5%, 6.25% and 3.125%), were applied to cultured murine fibroblasts (3T3), and viability was measured after 24-hour incubation by 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide assay. Viability of less than 70% was considered cytotoxic.

Results: CS extract showed cytotoxic effects at extract concentrations above 12.5% (viability:  $89.1\pm3.5\%$  at 3.125%,  $77.8\pm1.8\%$  at 6.25%,  $72.8\pm9.7\%$  at 12.5%,  $5.9\pm0.9\%$  at 25%,  $9.4\pm5.3\%$  at 50% and  $5.7\pm0.7\%$  at 100% extract concentration). Range of fibroblast viability for EC vapor extracts was 88.5-117.8% at 3.125%, 86.4-115.3% at 6.25%, 85.8-111.7% at 12.5%, 78.1-106.2% at 25%, 79.0-103.7% at 50% and 51.0-102.2% at 100% extract concentration. One vapor extract was cytotoxic at 100% extract concentration only (viability:  $51.0\pm2.6\%$ ). However, even for that liquid, viability was 795% higher relative to CS extract.

Conclusions: This study indicates that EC vapor is significantly less cytotoxic compared tobacco CS. These results should be validated by clinical studies.

http://www.tandfonline.com/doi/abs/10.3109/08958378.2013.793439

Metal and Silicate Particles Including Nanoparticles Are Present in Electronic Cigarette Cartomizer Fluid and Aerosol

Monique Williams,

- Amanda Villarreal,
- Krassimir Bozhilov,
- Sabrina Lin,
- Prue Talbot
  - Published: March 20, 2013

#### Abstract

#### Background

Electronic cigarettes (EC) deliver aerosol by heating fluid containing nicotine. Cartomizer EC combine the fluid chamber and heating element in a single unit. Because EC do not burn tobacco, they may be safer than conventional cigarettes. Their use is rapidly increasing worldwide with little prior testing of their aerosol.

#### Objectives

We tested the hypothesis that EC aerosol contains metals derived from various components in EC.

#### Methods

Cartomizer contents and aerosols were analyzed using light and electron microscopy, cytotoxicity testing, x-ray microanalysis, particle counting, and inductively coupled plasma optical emission spectrometry.

#### Results

The filament, a nickel-chromium wire, was coupled to a thicker copper wire coated with silver. The silver coating was sometimes missing. Four tin solder joints attached the wires to each other and coupled the copper/silver wire to the air tube and mouthpiece. All cartomizers had evidence of use before packaging (burn spots on the fibers and electrophoretic movement of fluid in the fibers). Fibers in two cartomizers had green deposits that contained copper. Centrifugation of the fibers produced large pellets containing tin. Tin particles and tin whiskers were identified in cartridge fluid and outer fibers. Cartomizer fluid with tin particles was cytotoxic in assays using human pulmonary fibroblasts. The aerosol contained particles >1 µm comprised of tin, silver, iron, nickel, aluminum, and silicate and nanoparticles (<100 nm) of tin, chromium and nickel. The concentrations of nine of eleven elements in EC aerosol were higher than or equal to the corresponding concentrations in conventional cigarette smoke. Many of the elements identified in EC aerosol are known to cause respiratory distress and disease.

#### Conclusions

The presence of metal and silicate particles in cartomizer aerosol demonstrates the need for improved quality control in EC design and manufacture and studies on how EC aerosol impacts the health of users and bystanders.

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0057987 Int. J. Environ. Res. Public Health 2013, 10(6), 2500-2514; doi:10.3390/ijerph10062500 Article

Evaluation of Electronic Cigarette Use (Vaping) Topography and Estimation of Liquid Consumption: Implications for Research Protocol Standards Definition and for Public Health Authorities' Regulation

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  Received: 18 May 2013 / Revised: 6 June 2013 / Accepted: 7 June 2013 / Published: 18 June 2013

#### **Abstract**

Background: Although millions of people are using electronic cigarettes (ECs) and research on this topic has intensified in recent years, the pattern of EC use has not been systematically studied. Additionally, no comparative measure of exposure and nicotine delivery between EC and tobacco cigarette or nicotine replacement therapy (NRTs) has been established. This is important, especially in the context of the proposal for a new Tobacco Product Directive issued by the European Commission Methods: A second generation EC device, consisting of a higher capacity battery and tank atomiser design compared to smaller cigarette-like batteries and cartomizers, and a 9 mg/mL nicotine-concentration liquid were used in this study. Eighty subjects were recruited; 45 experienced EC users and 35 smokers. EC users were video-recorded when using the device (ECIG group), while smokers were recorded when smoking (SM-S group) and when using the EC (SM-E group) in a randomized cross-over design. Puff, inhalation and exhalation duration were measured. Additionally, the amount of EC liquid consumed by experienced EC users was measured at 5 min (similar to the time needed to smoke one tobacco cigarette) and at 20 min (similar to the time needed for a nicotine inhaler to deliver 4 mg nicotine). Results: Puff duration was significantly higher in ECIG  $(4.2 \pm 0.7 \text{ s})$  compared to SM-S  $(2.1 \pm 0.4 \text{ s})$  and SM-E  $(2.3 \pm 0.5 \text{ s})$ , while inhalation time was lower (1.3  $\pm$  0.4, 2.1  $\pm$  0.4 and 2.1  $\pm$  0.4 respectively). No difference was observed in exhalation duration. EC users took 13 puffs and consumed 62 ± 16 mg liquid in 5 min; they took 43 puffs and consumed 219 ± 56 mg liquid in 20 min. Nicotine delivery was estimated at  $0.46 \pm 0.12$  mg after 5 min and  $1.63 \pm 0.41$  mg after 20 min of use. Therefore, 20.8 mg/mL and 23.8 mg/mL nicotine-containing liquids would deliver 1 mg of nicotine in 5 min and 4 mg nicotine in 20 min, respectively. Since the ISO method significantly underestimates nicotine delivery by tobacco cigarettes, it seems that liquids with even higher than 24 mg/mL nicotine concentration would be comparable to one tobacco cigarette. Conclusions: EC use topography is significantly different compared to smoking. Four-second puffs with 20-30 s interpuff interval should be used when assessing EC effects in laboratory experiments, provided that the equipment used does not get overheated. Based on the characteristics of the device used in this study, a 20 mg/mL nicotine concentration liquid would be needed in order to deliver nicotine at

amounts similar to the maximum allowable content of one tobacco cigarette (as measured by the ISO 3308 method). The results of this study do not support the statement of the European Commission Tobacco Product Directive that liquids with nicotine concentration of 4 mg/mL are comparable to NRTs in the amount of nicotine delivered to the user.

<u>Inhal Toxicol.</u> 2012 Oct;24(12):850-7. doi: 10.3109/08958378.2012.724728. Comparison of the effects of e-cigarette vapor and cigarette smoke on indoor air quality.

# McAuley TR1, Hopke PK, Zhao J, Babaian S. Author information

#### Abstract

#### CONTEXT:

Electronic cigarettes (e-cigarettes) have earned considerable attention recently as an alternative to smoking tobacco, but uncertainties about their impact on health and indoor air quality have resulted in proposals for bans on indoor e-cigarette use.

#### **OBJECTIVE:**

To assess potential health impacts relating to the use of e-cigarettes, a series of studies were conducted using e-cigarettes and standard tobacco cigarettes.

#### METHODS AND MATERIALS:

Four different high nicotine e-liquids were vaporized in two sets of experiments by generic 2-piece e-cigarettes to collect emissions and assess indoor air concentrations of common tobacco smoke by products. Tobacco cigarette smoke tests were conducted for comparison.

#### **RESULTS:**

Comparisons of pollutant concentrations were made between e-cigarette vapor and tobacco smoke samples. Pollutants included VOCs, carbonyls, PAHs, nicotine, TSNAs, and glycols. From these results, risk analyses were conducted based on dilution into a 40 m³ room and standard toxicological data. Non-cancer risk analysis revealed "No Significant Risk" of harm to human health for vapor samples from e-liquids (A-D). In contrast, for tobacco smoke most findings markedly exceeded risk limits indicating a condition of "Significant Risk" of harm to human health. With regard to cancer risk analysis, no vapor sample from e-liquids A-D exceeded the risk limit for either children or adults. The tobacco smoke sample approached the risk limits for adult exposure.

#### **CONCLUSIONS:**

For all byproducts measured, electronic cigarettes produce very small exposures relative to tobacco cigarettes. The study indicates no apparent risk to human health from e-cigarette emissions based on the compounds analyzed.

http://www.ncbi.nlm.nih.gov/pubmed/23033998

Safety Report on the Ruyan® e-cigarette Cartridge and Inhaled Aerosol Dr Murray Laugesen QSO, MBChB, FAFPHM, FRCS, Dip Obst

Health New Zealand Ltd Christchurch, New Zealand. <u>www.healthnz.co.nz</u> 30 October 2008

#### Summary

Aim. This report aims to assist regulators in initial assessment of the safety of the Ruyan® e-cigarette and its cartridges, and the possible risks and benefits from permitting its use.

Method. Health New Zealand Ltd contracted with seven leading government, university and commercial laboratories in New Zealand and Canada to independently perform various tests on the Ruyan cigarette's nicotine refill cartridge.

Findings. Ruyan® e-cigarette is designed to be a safe alternative to smoking. The various test results confirm this is the case. It is very safe relative to cigarettes, and also safe in absolute terms on all measurements we have applied. Using micro-electronics it vaporizes, separately for each puff, very small quantities of nicotine dissolved in propylene glycol, two small well-known molecules with excellent safety profiles, – into a fine aerosol. Each puff contains one third to one half the nicotine in a tobacco cigarette's puff. The cartridge liquid is tobacco-free and no combustion occurs.

Competency. The author has authored or co-authored over 30 research papers and reports in national and international scientific medical journals since 1995, on smoking, and latterly on testing of cigarettes and cigarette substitutes.

www.healthnz.co.nz/Publicnsall.htm

Financial disclosure. This report is funded by Ruyan. Disclaimer. Apart from research Health New Zealand derives no financial benefit from Ruyan.

Limitation. Unless the contrary is stated, findings refer specifically to Ruyan® ecigarettes only.

http://www.healthnz.co.nz/RuyanCartridgeReport30-Oct-08.pdf

<u>Life Sci.</u> 1996;58(16):1339-46. Long-term effects of inhaled nicotine. Waldum HL1, Nilsen OG, Nilsen T, Rørvik H, Syversen V, Sanvik AK, Haugen OA, Torp SH, Brenna E.

#### Abstract

Tobacco smoking has been reported to be associated with increased risk of cardiovascular disease and cancer, particularly of the lungs. In spite of extensive research on the health effects of tobacco smoking, the substances in tobacco smoke exerting these negative health effects are not completely known. Nicotine is the substance giving the subjective pleasure of smoking as well as inducing addiction. For the first time we report the effect on the rat of long-term (two years) inhalation of nicotine. The rats breathed in a chamber with nicotine at a concentration giving twice the plasma concentration found in heavy smokers. Nicotine was given for 20 h a day, five days a week during a two-year period. We could not find any increase in mortality, in atherosclerosis or frequency of tumors in these rats compared with controls. Particularly, there was no microscopic or macroscopic lung tumors nor any increase in pulmonary neuroendocrine cells. Throughout the study, however, the body weight of the nicotine exposed rats was reduced as compared with controls. In conclusion, our study does not indicate any harmful effect of nicotine when given in its pure form by inhalation.

http://www.ncbi.nlm.nih.gov/pubmed/8614291

### Research on Vaping as a Means of Reducing or Quitting Smoking

The below list is continually growing but is by no means exhaustive. Apologies to those whose studies I've yet to include - Jay Pieski

Study/Report

Date

Author

Key points

Italy: Quit and Smoking Mar 2015 J. Environ. Res. Reduction Rates in **Vape Shop Consumers** 

Public Health: Polosa et al

The researchers report the proportion of smokers who had quit smoking or reduced substantially (by 80% or more) at the one-year follow-up. The quit rate at one-year follow-up was 40.8%. The proportion of heavy reducers at one-year follow-up was 15.5%. Thus, the combined proportion of quitters and heavy reducers was 56.3%.

Web links: http://tobaccoanalysis.blogspot.com.au/2015/04/new-pilot-study-finds-high-cessation.html & http://www.mdpi.com/1660-4601/12/4/3428

E-cigarette preferred over Nicorette inhaler for smoking cessation (trial study)

Mar 2015 Steinberg et al

"More subjects would use the e-cigarette to make a quit attempt (76 %) than the inhaler (24 %).

18% (7/38) of subjects abstained from smoking during the 3-day periods using the e-cigarette vs. 10 % (4/38) using the inhaler."

Web link: http://www.ncbi.nlm.nih.gov/pubmed/24830741

England: Graph on support used in quit attempts

Feb 2015 Smoking Toolkit Study: West & Brown

Graph indicating the increase in vaping for smoking cessation, to near 1/3 of respondents in 2015, while cessation over the counter and prescription pharmaceuticals continue to decline.

Web link: https://9bc2db15-a-62cb3a1a-s-sites.googlegroups.com/site/vaperesearch/UKVapingCessation.PNG Source: http://www.smokinginengland.info/latest-statistics/

USA: Vape store customers: Verified smoking cessation and vaping beliefs

Feb 2015 Addiction: Tackett et al

Most vape store customers reported:

- starting vape systems as a means of smoking cessation (86%)
- using newer generation devices (89%). There was a high rate of switching (91.4%) to newer generation systems among those who started with a first generation (cigarette-like) product.
- vaping non-tobacco/non-menthol flavors (72%)
- using e-liquid with nicotine strengths of ≤20 mg/ml (72%).

Exhaled CO readings confirmed that 66% of the tested sample had quit smoking.

Among those who continued to smoke, mean cigarettes per day decreased from 22.1 to 7.5.

People who reported vaping longer, using newer generation devices and using non-tobacco and non-menthol flavors were more likely to have quit smoking.

Web link: http://onlinelibrary.wiley.com/doi/10.1111/add.12878/abstract

Electronic cigarettes for smoking cessation and reduction

Cochrane Library: Dec McRobbie et al 2014

Combined results from two studies, involving over 600 people, showed that using an EC containing nicotine increased the chances of stopping smoking long-term compared to using an EC without nicotine. This study showed that people who used EC were more likely to cut down the amount they smoked by at least half than people using a patch. The other studies were of lower quality, but they supported these findings.

Web link: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010216.pub2/abstract

Vaping less addictive than smoking

Dec 2014 et al

Penn State College "We found that e-cigarettes appear to be less addictive than tobacco of Medicine: Foulds cigarettes in a large sample of long-term users".

The researchers don't know why, but speculate that less nicotine is delivered, and suggest that more improved vaping devices may help more smokers give up.

The researchers don't comment on other chemicals in tobacco which may result in it being more addictive.

Web link: http://www.newswise.com/articles/e-cigarettes-less-addictive-than-cigarettes

Melbourne Study on cessation and reduction

Dec 2014 American Heart Assoc: Rahman et al

- Meta-analyses included 1,242 participants on whom complete smoking cessation data was available.
- The 1,242 smokers were attempting to guit using various (?) methods with some using e cigarettes
- Of all those followed, 224 (18%) reported smoking cessation after using nicotine-enriched e-cigarettes for a minimum period of six months...
- Nicotine filled e-cigarettes were more effective in achieving cessation compared to those without nicotine.
- Use of e-cigarettes was also effective in reducing smokers' daily cigarette consumption.

Web link: http://circ.ahajournals.org/content/130/Suppl\_2/A14945.short

Italian study of unwilling-toquit smokers

Nov 2014 Polosa et al

50 participants studied over 6 months

"The use of second generation PVs (personal vaporisers) substantially decreased cigarette consumption without causing significant adverse effects in smokers not intending to quit."

Web link: http://www.ncbi.nlm.nih.gov/pubmed/25380748

E-cigarette use in different regulatory environments UK and Australia

Nov 2014

Cancer Council Victoria, Kings College London, University of Waterloo

"While we await research findings on the efficacy and public health impact of ECs, smokers who are unwilling and/or unable to quit should be encouraged to try them where they are allowed on the basis that they are less harmful than continuing to smoke.

In our view, a case is continually building for Australia to find a regulatory mechanism to allow access to these products for smokers who may be interested in trying them as an alternative to smoking, if not as an alternative smoking cessation strategy."

Web link (full text by subscription only): http://ntr.oxfordjournals.org/content/early/2014/10/29/ntr.ntu231.abstract

Flemish study of unwilling-toquit smokers

Oct 2014 Adriaens et al.

48 participants (2 ecig groups, 1 control)

Participants unwilling to quit

Remarkable >50% reduction or complete abstinence from tobacco in almost half ecig participants after 8 months

Web link: http://www.mdpi.com/1660-4601/11/11/11220

E-cigs, Smoking Cessation and Motivation to Quit

Sep 2014

Biener et al

1,374 baseline cigarette smokers interviewed in 2011/2012.

Follow-up interviews conducted with 695 in 2014.

"Daily use of electronic cigarettes for at least 1 month is strongly

associated with guitting smoking at follow up."

Web link: http://ntr.oxfordjournals.org/content/early/2014/10/29/ntr.ntu200

Real-world effectiveness of ecigarettes

Sept 2014

Addiction: Brown et For smokers who choose to quit without professional support, e-cigarette users are more likely to report continued abstinence than NRT users (i.e.

gum, patch) or those who try unaided

Web link: http://onlinelibrary.wiley.com/doi/10.1111/add.12623/abstract

North Carolina Physicians' attitudes

Jul 2014 PLOS: Kandra et al "Two thirds (67%) of the surveyed physicians indicated e-cigarettes are a helpful aid for smoking cessation, and 35% recommended them to their patients."

Web link: http://www.plosone.org/article/info:doi/10.1371/journal.pone.0103462

Usage and concerns: 10,000+ vapers

Jul 2014 vaping.com: Neil Mclaren

As vapers move from disposable e-cigarettes to personal vaporisers there is a strong tendency to not/no longer smoke (51% versus 93%). Vapers who dual use (ie also smoke) tend to be more affected by negative media stories than those who don't.

Web link: http://vaping.com/data/vaping-survey-2014-initial-findings

potential for harm and benefit

E-cigarettes review and Jul 2014 Addiction: Hajek et "Allowing EC to compete with cigarettes in the market-place might decrease smoking-related morbidity and mortality. Regulating EC as strictly as cigarettes, or even more strictly as some regulators propose, is not warranted on current evidence.

> Health professionals may consider advising smokers unable or unwilling to quit through other routes to switch to EC as a safer alternative to smoking and a possible pathway to complete cessation of nicotine use."

Web link: http://onlinelibrary.wiley.com/doi/10.1111/add.12659/abstract

E-cigarettes & Public Health

May 2014 Public Health England: Britton & Bogdanovica

"Electronic cigarettes, and the various new generation nicotine devices in development, clearly have potential to reduce the prevalence of smoking in the UK. The challenges are to harness that potential, maximise the benefits, and minimise risks...

The optimum solution for population health is to maximise both the use of electronic cigarettes among smokers, and the proportion of users who engage with Stop Smoking Services (SSS). This will require some changes to current SSS practice. "

Web link: https://www.gov.uk/government/uploads/system/uploads/attachment\_data/file/311887/Ecigarettes\_report.pdf

Online survey of 19,441 Apr 2014 Farsalinos et al vapers worldwide

Worldwide survey in 10 languages Nearly all were former or current smokers (99.6%) Over 80% had completely ceased smoking

Others decreased daily smoking intake to one fifth previous levels

Web link: http://www.ecigarette-research.com/web/index.php/research/2014/161-survey-ecig

A longitudinal study of Feb 2014 Etter et al

electronic cigarette

users

users

367 over one year

477 users studied one month

E-cigarette use had no deleterious effects on smoking behaviour E-cigarettes may contribute to relapse prevention in former smokers and smoking cessation in current smokers.

Web link: http://www.sciencedirect.com/science/article/pii/S0306460313003304

Hawaii multiethnic study of e-cigarette Sept 2013

NCBI: Pohkrel et al "Cross-sectional data in 2010-2012 from 1567 adult daily smokers in

13% reported having ever used e-cigarettes to quit smoking. They reported higher motivation to quit, higher quitting self-efficacy, and longer recent guit duration than did other smokers."

http://www.ncbi.nlm.nih.gov/pubmed/23865700

NZ randomised controlled trial (2011-

Sept 2013

Lancet: Bullen et al 657 people randomised (289 to nicotine e-cigarettes, 295 to patches, and

73 to placebo e-cigarettes)

Abstinence at 6 months: 7.3% with nicotine e-cigarettes, 5.8% with

patches, and 4-1% with placebo e-cigarettes

Web link: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2813%2961842-5/abstract

Pilot study of unwilling-to-quit smokers given ecigarettes

Jul 2013 Wagener et al

20 smokers provided with e-cigarette and assessed after 1 week "Readiness and confidence to quit increased significantly during the experimentation period and continued to increase during use. Regular cigarette smoking was reduced by 44% from baseline.

Web link: http://intr.oxfordjournals.org/content/16/1/108.short

Trial of e-cigarette as tobacco cigarette

substitute

Jun 2013 Caponnetto et al

300 unwilling-to-quit smokers

12 month randomised, controlled trial

"In smokers not intending to quit, the use of e-cigarettes, with or without nicotine, decreased cigarette consumption and elicited enduring tobacco abstinence without causing significant side effects."

Web link: http://www.plosone.org/article/info:doi/10.1371/journal.pone.0066317

E-cigarette users (online survey)

Mar 2013 Addiction: Dawkins 1,347 respondents, 33 countries

et al

74% reported cessation for at least 3 weeks

70% reported reduced urge to smoke

Web link: http://onlinelibrary.wiley.com/doi/10.1111/add.12150/abstract

Views of aficionados and clinical/public health perspectives Aug Intl Journal of 2011 Clinical Practice: Foulds et al

104 experienced e-cig users

"Of all the e-cig users, 78% had not used any tobacco in the prior 30

days.

Three quarters started using e-cigs with the intention of quitting smoking and almost all felt that the e-cig had helped them to succeed in quitting

smoking

Only 8% were using the most widely sold types of cigarette-sized e-cig"

Web link: http://onlinelibrary.wiley.com/doi/10.1111/j.1742-1241.2011.02751.x/full



# Quit and Smoking Reduction Rates in Vape Shop Consumers: A Prospective 12-Month Survey

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#### **Abstract**

Aims: Here, we present results from a prospective pilot study that was aimed at surveying changes in daily cigarette consumption in smokers making their first purchase at vape shops. Modifications in products purchase were also noted. Design: Participants were instructed how to charge, fill, activate and use their e-cigarettes (e-cigs). Participants were encouraged to use these products in the anticipation of reducing the number of cig/day smoked. Settings: Staff from LIAF contacted 10 vape shops in the province of the city of Catania (Italy) that acted as sponsors to the 2013 No Tobacco Day. Participants: 71 adult smokers (≥18 years old) making their first purchase at local participating vape shops were asked by professional retail staff to complete a form. Measurements: Their cigarette consumption was followed-up prospectively at 6 and 12 months. Details of products purchase (i.e., e-cigs hardware, eliquid nicotine strengths and flavours) were also noted. Findings: Retention rate was elevated, with 69% of participants attending their final follow-up visit. At 12 month, 40.8% subjects could be classified as quitters, 25.4% as reducers and 33.8% as failures. Switching from standard refillables (initial choice) to more advanced devices (MODs) was observed in this study (from 8.5% at baseline to 18.4% at 12 month) as well as a trend in decreasing thee-liquid nicotine strength, with more participants adopting low nicotine strength (from 49.3% at baseline to 57.1% at 12 month). Conclusions: We have found that smokers purchasing e-cigarettes from vape shops with professional advice and support can achieve high success rates.

http://www.mdpi.com/1660-4601/12/4/3428

E-cigarette versus nicotine inhaler: comparing the perceptions and experiences of inhaled nicotine devices.

Steinberg MB1, Zimmermann MH, Delnevo CD, Lewis MJ, Shukla P, Coups EJ, Foulds J.

#### Abstract

#### BACKGROUND:

Novel nicotine delivery products, such as electronic cigarettes (e-cigarettes), have dramatically grown in popularity despite limited data on safety and benefit. In contrast, the similar U.S. Food and Drug Administration (FDA)-approved nicotine inhaler is rarely utilized by smokers. Understanding this paradox could be helpful to determine the potential for e-cigarettes as an alternative to tobacco smoking.

#### **OBJECTIVE:**

To compare the e-cigarette with the nicotine inhaler in terms of perceived benefits, harms, appeal, and role in assisting with smoking cessation.

#### **DESIGN:**

A cross-over trial was conducted from 2012 to 2013 PARTICIPANTS/INTERVENTIONS: Forty-one current smokers age 18 and older used the e-cigarette and nicotine inhaler each for 3 days, in random order, with a washout period in between. Thirty-eight participants provided data on product use, perceptions, and experiences.

#### MAIN MEASURES:

The Modified Cigarette Evaluation Questionnaire (mCEQ) measured satisfaction, reward, and aversion. Subjects were also asked about each product's helpfulness, similarity to cigarettes, acceptability, image, and effectiveness in quitting smoking. Cigarette use was also recorded during the product-use periods. KEY RESULTS:

The e-cigarette had a higher total satisfaction score (13.9 vs. 6.8 [p < 0.001]; range for responses 3-21) and higher reward score (15.8 vs. 8.7 [p < 0.001]; range for responses 5-35) than the inhaler. The e-cigarette received higher ratings for helpfulness, acceptability, and "coolness." More subjects would use the e-cigarette to make a quit attempt (76 %) than the inhaler (24 %) (p < 0.001). Eighteen percent (7/38) of subjects abstained from smoking during the 3-day periods using the e-cigarette vs. 10 % (4/38) using the inhaler (p = 0.18).

#### CONCLUSION:

The e-cigarette was more acceptable, provided more satisfaction, and had higher perceived benefit than the inhaler during this trial. E-cigarettes have the potential to be important nicotine delivery products

owing to their high acceptance and perceived benefit, but more data are needed to evaluate their actual efficacy and safety. Providers should be aware of these issues, as patients will increasingly inquire about them.

http://www.ncbi.nlm.nih.gov/pubmed/24830741

Biochemically verified smoking cessation and vaping beliefs among vape store customers

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#### Abstract

#### Aims

To evaluate biochemically verified smoking status and electronic nicotine delivery systems (ENDS) use behaviors and beliefs among a sample of customers from vapor stores (stores specializing in ENDS).

Design, Setting and Participants

A cross-sectional survey of 215 adult vapor store customers at four retail locations in the Midwestern United States; a subset of participants (n = 181) also completed exhaled carbon monoxide (CO) testing to verify smoking status.

#### Measurements

Outcomes evaluated included ENDS preferences, harm beliefs, use behaviors, smoking history and current biochemically verified smoking status.

#### **Findings**

Most customers reported starting ENDS as a means of smoking cessation (86%), using newer-generation devices (89%), vaping non-tobacco/non-menthol flavors (72%) and using e-liquid with nicotine strengths of  $\leq$ 20 mg/ml (72%). There was a high rate of switching (91.4%) to newer-generation ENDS among those who started with a first-generation product. Exhaled CO readings confirmed that 66% of the tested sample had quit smoking. Among those who continued to smoke, mean cigarettes per day decreased from 22.1 to 7.5 (P <0.001). People who reported vaping longer [odds ratio (OR) = 4.659, 95% confidence interval (CI) = 2.001–10.846], using newer-generation devices (OR = 2.950, 95% CI = 1.037–8.395) and

using non-tobacco and non-menthol flavors (OR = 2.626, 95% CI = 1.133-6.085) were more likely to have quit smoking.

Conclusions

Among vapor store customers in the United States who use electronic nicotine delivery devices to stop smoking, vaping longer, using newer-generation devices and using non-tobacco and non-menthol flavored e-liquid appear to be associated with higher rates of smoking cessation.

http://onlinelibrary.wiley.com/doi/10.1111/add.12878/abstract

## Electronic cigarettes for smoking cessation and reduction

Hayden McRobbie1,\*, Chris Bullen2, Jamie Hartmann-Boyce3, Peter Hajek1

Editorial Group: Cochrane Tobacco Addiction Group

#### Abstract

Background

Electronic cigarettes (ECs) are electronic devices that heat a liquid - usually comprising propylene glycol and glycerol, with or without nicotine and flavours, stored in disposable or refillable cartridges or a reservoir - into an aerosol for inhalation. Since ECs appeared on the market in 2006 there has been a steady growth in sales. Smokers report using ECs to reduce risks of smoking, but some healthcare organisations have been reluctant to encourage smokers to switch to ECs, citing lack of evidence of efficacy and safety. Smokers, healthcare providers and regulators are interested to know if these devices can reduce the harms associated with smoking. In particular, healthcare providers have an urgent need to know what advice they should give to smokers enquiring about ECs.

Objectives

To examine the efficacy of ECs in helping people who smoke to achieve long-term abstinence; to examine the efficacy of ECs in helping people reduce cigarette consumption by at least 50% of baseline levels; and to assess the occurrence of adverse events associated with EC use.

Search methods

We searched the Cochrane Tobacco Addiction Groups Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, and two other databases for relevant records from 2004 to July 2014, together with reference checking and contact with study authors.

#### Selection criteria

We included randomized controlled trials (RCTs) in which current smokers (motivated or unmotivated to quit) were randomized to EC or a control condition, and which measured abstinence rates or changes in cigarette consumption at six months or longer. As the field of EC research is new, we also included cohort follow-up studies with at least six months follow-up. We included randomized cross-over trials and cohort follow-up studies that included at least one week of EC use for assessment of adverse events.

#### Data collection and analysis

One review author extracted data from the included studies and another checked them. Our main outcome measure was abstinence from smoking after at least six months follow-up, and we used the most rigorous definition available (continuous, biochemically validated, longest follow-up). For reduction we used a dichotomous approach (no change/reduction < 50% versus reduction by 50% or more of baseline cigarette consumption). We used a fixed-effect Mantel-Haenszel model to calculate the risk ratio (RR) with a 95% confidence interval (CI) for each study, and where appropriate we pooled data from these studies in meta-analyses.

#### Main results

Our search identified almost 600 records, from which we include 29 representing 13 completed studies (two RCTs, 11 cohort). We identified nine ongoing trials. Two RCTs compared EC with placebo (non-nicotine) EC, with a combined sample size of 662 participants. One trial included minimal telephone support and one recruited smokers not intending to quit, and both used early EC models with low nicotine content. We judged the RCTs to be at low risk of bias, but under the GRADE system the overall quality of the evidence for our outcomes was rated 'low' or 'very low' because of imprecision due to the small number of trials. A 'low' grade means that further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. A 'very low' grade means we are very uncertain about the estimate. Participants using an EC were more likely to have abstained from smoking for at least six months compared with participants using placebo EC (RR

2.29, 95% CI 1.05 to 4.96; placebo 4% versus EC 9%; 2 studies; GRADE: low). The one study that compared EC to nicotine patch found no significant difference in six-month abstinence rates, but the confidence intervals do not rule out a clinically important difference (RR 1.26, 95% CI: 0.68 to 2.34; GRADE: very low). A higher number of people were able to reduce cigarette consumption by at least half with ECs compared with placebo ECs (RR 1.31, 95% CI 1.02 to 1.68, 2 studies; placebo: 27% versus EC: 36%; GRADE: low) and compared with patch (RR 1.41, 95% CI 1.20 to 1.67, 1 study; patch: 44% versus EC: 61%; GRADE: very low). Unlike smoking cessation outcomes, reduction results were not biochemically verified.

None of the RCTs or cohort studies reported any serious adverse events (SAEs) that were considered to be plausibly related to EC use. One RCT provided data on the proportion of participants experiencing any adverse events. Although the proportion of participants in the study arms experiencing adverse events was similar, the confidence intervals are wide (ECs vs placebo EC RR 0.97, 95% CI 0.71 to 1.34; ECs vs patch RR 0.99, 95% CI 0.81 to 1.22). The other RCT reported no statistically significant difference in the frequency of AEs at three- or 12-month follow-up between the EC and placebo EC groups, and showed that in all groups the frequency of AEs (with the exception of throat irritation) decreased significantly over time.

#### Authors' conclusions

There is evidence from two trials that ECs help smokers to stop smoking long-term compared with placebo ECs. However, the small number of trials, low event rates and wide confidence intervals around the estimates mean that our confidence in the result is rated 'low' by GRADE standards. The lack of difference between the effect of ECs compared with nicotine patches found in one trial is uncertain for similar reasons. ECs appear to help smokers unable to stop smoking altogether to reduce their cigarette consumption when compared with placebo ECs and nicotine patches, but the above limitations also affect certainty in this finding. In addition, lack of biochemical assessment of the actual reduction in smoke intake further limits this evidence. No evidence emerged that short-term EC use is associated with health risk.

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010216.pub2/abstract

Core 2. Epidemiology and Prevention of CV Disease: Physiology, Pharmacology and Lifestyle

Session Title: Behavioral Risk Factors and CVD Risk II

Abstract 14945: Electronic Cigarettes Are Effective for Smoking Cessation: Evidence From a

Systematic Review and Meta-analysis

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Abstract

Introduction: Smoking is the leading cause of preventable death worldwide. Finding effective interventions for smoking cessation has proven difficult and existing interventions have limited consumer appeal. Electronic cigarettes (e-cigarettes) are becoming increasingly popular and a possible role for them in smoking cessation is being debated. Our objective was therefore to analyse existing research to investigate whether use of e-cigarettes is an effective smoking cessation method.

Hypothesis: We assessed the hypothesis that use of e-cigarettes is an effective smoking cessation method.

Methods: A systematic review of articles in English of any publication date was conducted by searching PubMed, Web of Knowledge and Scopus databases. Published studies investigating the effectiveness of e-cigarettes for smoking cessation among current smokers were included. Studies were systematically reviewed, and meta-analyses were conducted using the Mantel-Haenszel fixed-effect and random-effects models. Heterogeneity and quality of the selected studies were also evaluated.

Results: Six studies were selected, including two randomised controlled trials, two cohort studies and two cross-sectional studies, and included 7,551 participants. Meta-analyses included 1,242 participants on whom complete smoking cessation data was available. Of these, 224 (18%) reported smoking cessation after using nicotine-enriched e-cigarettes for a minimum period of six months. Use of such e-

cigarettes was positively associated with smoking cessation with a pooled Effect Size of 0.20 (95%CI 0.11-0.28). Nicotine filled e-cigarettes were more effective in achieving cessation compared to

those without nicotine (pooled Risk Ratio 2.29, 95%CI 1.05-4.97). Use of e-cigarettes was also effective in reducing smokers' daily cigarette consumption. The studies included were heterogeneous, (I2=93%, p<0.001). A meta-regression model showed that 98% of this heterogeneity was caused by study design and gender variation.

Conclusions: In conclusion, available literature suggests that the use of e-cigarettes may be an effective alternate smoking cessation method. Further research is required to investigate this among both genders.

# E-Cigarettes Less Addictive Source Newsroom: Penn State Milton S. Hershey Medical CenterThan Cigarettes

Source Newsroom: Penn State Milton S. Hershey Medical Center

Newswise — E-cigarettes appear to be less addictive than cigarettes in former smokers and this could help improve understanding of how various nicotine delivery devices lead to dependence, according to researchers.

"We found that e-cigarettes appear to be less addictive than tobacco cigarettes in a large sample of long-term users," said Jonathan Foulds, Ph.D., professor of public health sciences and psychiatry, Penn State College of Medicine.

The popularity of e-cigarettes, which typically deliver nicotine, propylene glycol, glycerin and flavorings through inhaled vapor, has increased in the past five years. There are currently more than 400 brands of "e-cigs" available. E-cigs contain far fewer cancer-causing and other toxic substances than cigarettes, however their long-term effects on health and nicotine dependence are unknown.

To study e-cigarette dependence, the researchers developed an online survey, including questions designed to assess previous dependence on cigarettes and almost identical questions to assess current dependence on e-cigs. More than 3,500 current users of e-cigs who were ex-cigarette smokers completed the Penn State Cigarette Dependence Index and the Penn State Electronic Cigarette Dependence Index.

Higher nicotine concentration in e-cig liquid, as well as use of advanced second-generation e-cigs, which deliver nicotine more efficiently than earlier "cigalikes," predicted dependence. Consumers who had used e-cigs longer also appeared to be more addicted.

"However, people with all the characteristics of a more dependent e-cig user (e.g. longer use of an advanced e-cig with a high nicotine concentration in the liquid) in our study still had a lower e-cig dependence score than their cigarette dependence score," Foulds said. "We think this is because they're getting less nicotine from the e-cigs than they were getting from cigarettes."

Although many regular users of e-cigarettes are trying to quit smoking, the Food and Drug Administration has not approved them for this use, and they cannot be marketed as a smoking cessation product.

"This is a new class of products that's not yet regulated," Foulds said. "It has the potential to do good and help a lot of people quit, but it also has the potential to do harm. Continuing to smoke and use ecigarettes may not reduce health risks. Kids who have never smoked might begin nicotine addiction with e-cigs. There's a need for a better understanding of these products.

"We don't have long-term health data of e-cig use yet, but any common sense analysis says that e-cigs are much less toxic. And our paper shows that they appear to be much less addictive, as well. So in both measures they seem to have advantages when you're concerned about health."

The findings, which are published in Nicotine & Tobacco Research, also have implications for developing e-cigs for smoking cessation.

"We might actually need e-cigarettes that are better at delivering nicotine because that's what's more likely to help people quit," Foulds said.

Previous research shows that nicotine replacement efficacy correlates with higher nicotine dose and faster delivery speed.

The new index used in the study is more modern than the most widely-used dependence survey, the Fagerstrom Test for Nicotine Dependence. That scale was developed 25 years ago and does not reflect modern use of tobacco and nicotine products.

"People smoke fewer cigarettes today but are still clearly addicted, and the old scale—while still reasonably effective—was not designed to measure that," Foulds said.

The new questionnaire also allows for cross-comparisons between different nicotine and tobacco products.

"Not only are e-cigs a booming industry, but new tobacco products are set to enter the market soon," Foulds said. "Our questionnaire is designed to compare dependence across different products simply by substituting the different product name into the questionnaire in place of cigarettes."

Additional researchers on this project are Susan Veldheer, research coordinator, Jessica Yingst, research assistant, and Shari Hrabovsky, research nurse practitioner, all at Penn State College of Medicine; Stephen J. Wilson and Travis T. Nichols, both at Penn State; and Thomas T. Eissenberg at Virginia Commonwealth University.

This work was initially funded by an internal grant from Penn State Social Science Research Institute and Cancer Institute, the National Institute on Drug Abuse of the National Institutes of Health and the Center for Tobacco Products of the U.S. Food and Drug Administration. (P50-DA-036107-01, P50-DA-036105. P50DA036105)

Located on the campus of Penn State Milton S. Hershey Medical Center in Hershey, Pa., Penn State College of Medicine boasts a portfolio of nearly \$82 million in funded research. Projects range from the development of artificial organs and advanced diagnostics to groundbreaking cancer treatments and understanding the fundamental causes of disease. Enrolling its first students in 1967, the College of Medicine has more than 1,600 students and trainees in medicine, nursing, the health professions and biomedical research on its campus.

http://www.newswise.com/articles/e-cigarettes-less-addictive-than-cigarettes

Success rates with nicotine personal vaporizers: a prospective 6-month pilot study of smokers not intending to quit.

Polosa R1, Caponnetto P, Maglia M, Morjaria JB, Russo C.

Author information

Abstract

**BACKGROUND:** 

Electronic cigarettes (e-Cigs) are an attractive long-term alternative nicotine source to conventional cigarettes. Although they may assist smokers to remain abstinent during their quit attempt, studies using first generation e-Cigs report low success rates. Second generation devices (personal vaporisers - PVs) may result in much higher quit rates, but their efficacy and safety in smoking cessation and/or reduction in clinical trials is unreported.

#### METHOD:

We conducted a prospective proof-of-concept study monitoring modifications in smoking behaviour of 50 smokers (unwilling to quit) switched onto PVs. Participants attended five study visits: baseline, week-4, week-8, week-12 and week-24. Number of cigarettes/day (cigs/day) and exhaled carbon monoxide (eCO) levels were noted at each visit. Smoking reduction/abstinence rates, product usage, adverse events and subjective opinions of these products were also reviewed.

#### **RESULTS:**

Sustained 50% and 80% reduction in cigs/day at week-24 was reported in 15/50 (30%) and 7/50 (14%) participants with a reduction from 25cigs/day to 6cigs/day (p < 0.001) and 3cigs/day (p < 0.001), respectively. Smoking abstinence (self-reported abstinence from cigarette smoking verified by an eCO  $\leq$ 10 ppm) at week-24 was observed in 18/50 (36%) participants, with 15/18 (83.3%) still using their PVs at the end of the study. Combined 50% reduction and smoking abstinence was shown in 33/50 (66%) participants. Throat/mouth irritation (35.6%), dry throat/mouth (28.9%), headache (26.7%) and dry cough (22.2%) were frequently reported early in the study, but waned substantially by week-24. Participants' perception and acceptance of the products was very good.

## **CONCLUSION:**

The use of second generation PVs substantially decreased cigarette consumption without causing significant adverse effects in smokers not intending to quit.

http://www.ncbi.nlm.nih.gov/pubmed/25380748

# E-cigarette use in different regulatory environments UK and Australia

Trends in e-cigarette awareness, trial, and use under the different regulatory environments of Australia and the UK

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# Abstract

Introduction: E-cigarettes (ECs) have gained significant attention in recent years. They have been introduced in jurisdictions with divergent existing laws that affect their legality. This provides the opportunity for natural experiments to assess effects of such laws in some cases independent of any formulated government policy. We compare patterns of EC awareness and use over a three year period in Australia where laws severely restrict EC availability, with awareness and use in the UK where ECs are readily available.

Methods: Data analysed come from Waves 8 and 9 (collected in 2010 and 2013, respectively) of the International Tobacco Control (ITC) surveys in Australia and the UK (approximately 1500 respondents per wave per country).

Results: Across both waves, EC awareness, trial, and use among current and former smokers was significantly greater in the UK than in Australia, but all three of these measures increased significantly between 2010 and 2013 in both countries, and the rate of increase was equivalent between countries. 73% of UK respondents reported that their current brands contained nicotine as did 43% in Australia even though sale, possession and/or use of nicotine-containing ECs without a permit is illegal in Australia. EC use was greater among smokers in both countries, at least in part due to less uptake by ex-smokers.

Conclusions: EC awareness and use have risen rapidly between 2010 and 2013 among current and former smokers in both Australia and the UK despite different EC regulatory environments. Substantial numbers in both countries are using ECs that contain nicotine.

http://ntr.oxfordjournals.org/content/early/2014/10/29/ntr.ntu231.abstract

Effectiveness of the Electronic Cigarette: An Eight-Week Flemish Study with Six-Month Follow-up on Smoking Reduction, Craving and Experienced Benefits and Complaints

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# **Abstract**

Background: Smoking reduction remains a pivotal issue in public health policy, but quit rates obtained with traditional quit-smoking therapies remain disappointingly low. Tobacco Harm Reduction (THR), aiming at less harmful ways of consuming nicotine, may provide a more effective alternative. One promising candidate for THR are electronic cigarettes (e-cigs). The aim of this study was to investigate the efficacy of second-generation e-cigs both in terms of acute craving-reduction in the lab and in terms of smoking reduction and experienced benefits/complaints in an eight-month Randomized Controlled Trial (RCT). Design: RCT with three arms. Methods: Participants (N = 48) unwilling to quit smoking were randomized into two e-cig groups and one control group. During three lab sessions (over two months) participants, who had been abstinent for four hours, vaped/smoked for five minutes, after which we monitored the effect on craving and withdrawal symptoms. eCO and saliva cotinine levels were

also measured. In between lab sessions, participants in the e-cig groups could use e-cigs or smoke ad libitum, whereas the control group could only smoke. After the lab sessions, the control group also received an e-cig. The RCT included several questionnaires, which repeatedly monitored the effect of ad libitum e-cig use on the use of tobacco cigarettes and the experienced benefits/complaints up to six months after the last lab session. Results: From the first lab session on, e-cig use after four hours of abstinence resulted in a reduction in cigarette craving which was of the same magnitude as when a cigarette was smoked, while eCO was unaffected. After two months, we observed that 34% of the e-cig groups had stopped smoking tobacco cigarettes, versus 0% of the control group (difference p < 0.01). After five months, the e-cig groups demonstrated a total quit-rate of 37%, whereas the control group showed a quit rate of 38% three months after initiating e-cig use. At the end of the eight-month study, 19% of the e-cig groups and 25% of the control group were totally abstinent from smoking, while an overall reduction of 60% in the number of cigarettes smoked per day was observed (compared to intake). eCO levels decreased, whereas cotinine levels were the same in all groups at each moment of measurement. Reported benefits far outweighed the reported complaints. Conclusion: In a series of controlled lab sessions with e-cig naïve tobacco smokers, second generation e-cigs were shown to be immediately and highly effective in reducing abstinence induced cigarette craving and withdrawal symptoms, while not resulting in increases in eCO. Remarkable (>50 pc) eight-month reductions in, or complete abstinence from tobacco smoking was achieved with the e-cig in almost half (44%) of the participants.

http://www.mdpi.com/1660-4601/11/11/11220

A Longitudinal Study of Electronic Cigarette Use in a Population-Based Sample of Adult Smokers: Association With Smoking Cessation and Motivation to Quit

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# Abstract

Aims: Increasingly popular electronic cigarettes (e-cigarettes) may be the most promising development yet to end cigarette smoking. However, there is sparse evidence that their use promotes cessation. We investigated whether e-cigarette use increases smoking cessation and/or has a deleterious effect on quitting smoking and motivation to quit.

Methods: Representative samples of adults in 2U.S. metropolitan areas were surveyed in 2011/2012 about their use of novel tobacco products. In 2014, follow-up interviews were conducted with 695 of the 1,374 baseline cigarette smokers who had agreed to be re-contacted (retention rate: 51%). The follow-up interview assessed their smoking status and history of electronic cigarette usage. Respondents were categorized as intensive users (used e-cigarettes daily for at least 1 month), intermittent users (used regularly, but not daily for more than 1 month), and non-users/triers (used e-cigarettes at most once or twice).

Results: At follow-up, 23% were intensive users, 29% intermittent users, 18% had used once or twice, and 30% had not tried e-cigarettes. Logistic regression controlling for demographics and tobacco dependence indicated that intensive users of e-cigarettes were 6 times as likely as non-users/triers to report that they quit smoking (OR: 6.07, 95% CI = 1.11, 33.2). No such relationship was seen for intermittent users. There was a negative association between intermittent e-cigarette use and one of two indicators of motivation to quit at follow-up.

Conclusions: Daily use of electronic cigarettes for at least 1 month is strongly associated with quitting smoking at follow up. Further investigation of the underlying reasons for intensive

versus intermittent use will help shed light on the mechanisms underlying the associations between e-cigarette use, motivation to quit and smoking cessation.

http://ntr.oxfordjournals.org/content/early/2014/10/29/ntr.ntu200

Real-world effectiveness of e-cigarettes when used to aid smoking cessation: a cross-sectional population study

Jamie Brown1,2,\*, Emma Beard1, Daniel Kotz1,3, Susan Michie2,4 and Robert West1,4

# **Abstract**

**Background and Aims** 

Electronic cigarettes (e-cigarettes) are rapidly increasing in popularity. Two randomized controlled trials have suggested that e-cigarettes can aid smoking cessation, but there are many factors that could influence their real-world effectiveness. This study aimed to assess, using an established methodology, the effectiveness of e-cigarettes when used to aid smoking cessation compared with nicotine replacement therapy (NRT) bought over-the-counter and with unaided quitting in the general population.

# Design and Setting

A large cross-sectional survey of a representative sample of the English population.

# **Participants**

The study included 5863 adults who had smoked within the previous 12 months and made at least one quit attempt during that period with either an e-cigarette only (n = 464), NRT bought over-the-counter only (n = 1922) or no aid in their most recent quit attempt (n = 3477).

#### Measurements

The primary outcome was self-reported abstinence up to the time of the survey, adjusted for key potential confounders including nicotine dependence.

# **Findings**

E-cigarette users were more likely to report abstinence than either those who used NRT bought over-the-counter [odds ratio (OR) = 2.23, 95% confidence interval (CI) = 1.70-2.93, 20.0 versus 10.1%] or no aid (OR = 1.38, 95% CI = 1.08-1.76, 20.0 versus 15.4%). The adjusted odds of non-smoking in users of e-cigarettes were 1.63 (95% CI = 1.17-2.27) times higher compared with users of NRT bought over-the-counter and 1.61 (95% CI = 1.19-2.18) times higher compared with those using no aid.

# Conclusions

Among smokers who have attempted to stop without professional support, those who use e-cigarettes are more likely to report continued abstinence than those who used a licensed NRT product bought over-the-counter or no aid to cessation. This difference persists after adjusting for a range of smoker characteristics such as nicotine dependence.

http://onlinelibrary.wiley.com/doi/10.1111/add.12623/abstract

Physicians' Attitudes and Use of E-Cigarettes as Cessation Devices, North Carolina, 2013

Kelly L. Kandra, Leah M. Ranney, Joseph G. L. Lee, Adam O. Goldstein

# **Abstract**

### Introduction

Electronic cigarettes (e-cigarettes) are not currently approved or recommended by the Food and Drug Administration (FDA) or various medical organizations; yet, they appear to play a substantial role in tobacco users' cessation attempts. This study reports on a physician survey that measured beliefs, attitudes, and behavior related to e-cigarettes and smoking cessation. To our knowledge this is the first study to measure attitudes toward e-cigarettes among physicians treating adult smokers.

#### Methods

Using a direct marketing company, a random sample of 787 North Carolina physicians were contacted in 2013 through email, with 413 opening the email and 128 responding (response rate = 31%). Physicians' attitudes towards e-cigarettes were measured through a series of close-ended questions. Recommending e-cigarettes to patients served as the outcome variable for a logistic regression analysis.

#### Results

Two thirds (67%) of the surveyed physicians indicated e-cigarettes are a helpful aid for smoking cessation, and 35% recommended them to their patients. Physicians were more likely to recommend e-cigarettes when their patients asked about them or when the physician believed e-cigarettes were safer than smoking standard cigarettes.

## Conclusions

Many North Carolina physicians are having conversations about e-cigarettes with their patients, and some are recommending them. Future FDA regulation of e-cigarettes may help provide evidence-based guidance to physicians about e-cigarettes and will help ensure that patients receive evidence-based recommendations about the safety and efficacy of e-cigarettes in tobacco cessation.

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0103462

Electronic cigarettes: review of use, content, safety, effects on smokers and potential for harm and benefit

Peter Hajek1, Jean-François Etter2, Neal Benowitz3, Thomas Eissenberg4 and Hayden McRobbie1,\*

# **Abstract**

Aims

We reviewed available research on the use, content and safety of electronic cigarettes (EC), and

on their effects on users, to assess their potential for harm or benefit and to extract evidence

that can guide future policy.

Methods

Studies were identified by systematic database searches and screening references to February

2014.

Results

EC aerosol can contain some of the toxicants present in tobacco smoke, but at levels which are

much lower. Long-term health effects of EC use are unknown but compared with cigarettes, EC

are likely to be much less, if at all, harmful to users or bystanders. EC are increasingly popular

among smokers, but to date there is no evidence of regular use by never-smokers or by non-

smoking children. EC enable some users to reduce or quit smoking.

Conclusions

Allowing EC to compete with cigarettes in the market-place might decrease smoking-related

morbidity and mortality. Regulating EC as strictly as cigarettes, or even more strictly as some

regulators propose, is not warranted on current evidence. Health professionals may consider

advising smokers unable or unwilling to quit through other routes to switch to EC as a safer

alternative to smoking and a possible pathway to complete cessation of nicotine use.

http://onlinelibrary.wiley.com/doi/10.1111/add.12659/abstract

A report commissioned by Public Health

England

Authors: Professor John Britton and Dr Ilze Bogdanovica

**UK Centre for Tobacco and Alcohol Studies** 

Division of Epidemiology and Public Health, University of Nottingham

<a href="https://www.gov.uk/government/uploads/system/uploads/attachment\_data/file/311887/Ecig">https://www.gov.uk/government/uploads/system/uploads/system/uploads/attachment\_data/file/311887/Ecig</a>

arettes report.pdf

Switching from cigarettes to e-cigarettes has significant health benefits, according to a survey of more than 19,000 users

Many health benefits are reported by e-cigarette users, according to a new study published today in International Journal of Environmental Research and Public Health. The study was a worldwide survey, with a questionnaire available in 10 different languages, to assess the experience, patterns of use, side effect and benefits observed by e-cigarette consumers.

In total, 19,441 vapers participated to the study. More than 80% had completely substituted smoking with e-cigarette use, while the rest reduced smoking consumption from 20 to 4 tobacco cigarettes per day. The main findings of the survey were that vapers use e-cigarettes in order to reduce or completely substitute smoking for health reasons. They initiate use with high levels of nicotine, with more than 1 in 5 participants starting with higher than 20mg/ml nicotine concentration. E-cigarettes were effective smoking substitutes even with those with high-dependence on smoking, with most consumers using 2nd and 3rd generation devices. More than half reported side-effects; they were mild and temporary in most cases, with the most common symptom being dry mouth and throat. Importantly, significant benefits were reported for physiologic functions (such as better breathing, gustatory and olfactory senses), as well as improvements in pre-existing disease conditions (mainly respiratory disease, hypertension and hypercholesterolemia).

"This is by far the largest survey of e-cigarette users ever published until now" said leading researcher and main author of the manuscript Dr Konstantinos Farsalinos from the Onassis Cardiac Surgery Center in Athens-Greece. He noted: "Although the study evaluated the experience of dedicated users only, it is important to examine how this group is using e-

cigarettes so that we can instruct smokers on how to successfully use the devices in order to switch from tobacco to e-cigarette use."

The study found that those who completely substituted smoking were more likely to experience health benefits compared to dual users. "This is an expected finding", said Dr Farsalinos. "Ecigarettes do not have therapeutic properties, but using them instead of tobacco is definitely expected to result in substantial health benefits. This is supported from all research performed until now on the safety profile of e-cigarettes. However, we should wait for long-term follow-up studies to define the overall health impact of e-cigarette use."

A very small minority (0.4%) reported not being smokers at the time of initiation of EC use. They were consuming less liquid and were using lower nicotine levels; more than half of them were using non-nicotine liquids. "This is a very small minority of e-cigarette users, consistent with other studies showing minimal adoption by non-smokers", said Dr Farsalinos. "It should be emphasized that none of them became a smoker after initiating e-cigarette use, debunking the theory of gateway to smoking", he added.

http://www.ecigarette-research.com/web/index.php/research/2014/161-survey-ecig

A longitudinal study of electronic cigarette users

Jean-François Ettera, , , Chris Bullen

# **Abstract**

Objective

To assess behavior change over 12 months in users of e-cigarettes ("vapers").

#### Methods

Longitudinal Internet survey, 2011 to 2013. Participants were enrolled on websites dedicated to e-cigarettes and smoking cessation. We assessed use of e-cigarettes and tobacco among the same cohort at baseline, after one month (n = 477) and one year (n = 367).

#### Results

Most participants (72%) were former smokers, and 76% were using e-cigarettes daily. At baseline, current users had been using e-cigarettes for 3 months, took 150 puffs/day on their e-cigarette and used refill liquids containing 16 mg/ml of nicotine, on average. Almost all the daily vapers at baseline were still vaping daily after one month (98%) and one year (89%). Of those who had been vaping daily for less than one month at baseline, 93% were still vaping daily after one month, and 81% after one year. In daily vapers, the number of puffs/day on e-cigarettes remained unchanged between baseline and one year. Among former smokers who were vaping daily at baseline, 6% had relapsed to smoking after one month and also 6% after one year. Among dual users (smokers who were vaping daily at baseline), 22% had stopped smoking after one month and 46% after one year. In dual users who were still smoking at follow-up, cigarette consumption decreased by 5.3 cig/day after one month (from 11.3 to 6.0 cig./day, p = 0.006), but remained unchanged between baseline and 1-year follow-up.

# Conclusions

E-cigarettes may contribute to relapse prevention in former smokers and smoking cessation in current smokers.

http://www.sciencedirect.com/science/article/pii/S0306460313003304

Smokers who try e-cigarettes to quit smoking: findings from a multiethnic study in Hawaii.

Pokhrel P1, Fagan P, Little MA, Kawamoto CT, Herzog TA.

# **Abstract**

#### **OBJECTIVES:**

We characterized smokers who are likely to use electronic or "e-"cigarettes to quit smoking. METHODS:

We obtained cross-sectional data in 2010-2012 from 1567 adult daily smokers in Hawaii using a paper-and-pencil survey. Analyses were conducted using logistic regression.

# **RESULTS:**

Of the participants, 13% reported having ever used e-cigarettes to quit smoking. Smokers who had used them reported higher motivation to quit, higher quitting self-efficacy, and longer recent quit duration than did other smokers. Age (odds ratio [OR] = 0.98; 95% confidence interval [CI] = 0.97, 0.99) and Native Hawaiian ethnicity (OR = 0.68; 95% CI = 0.45, 0.99) were inversely associated with increased likelihood of ever using e-cigarettes for cessation. Other significant correlates were higher motivation to quit (OR = 1.14; 95% CI = 1.08, 1.21), quitting self-efficacy (OR = 1.18; 95% CI = 1.06, 1.36), and ever using US Food and Drug Administration (FDA)-approved cessation aids such as nicotine gum (OR = 3.72; 95% CI = 2.67, 5.19).

# **CONCLUSIONS:**

Smokers who try e-cigarettes to quit smoking appear to be serious about wanting to quit. Despite lack of evidence regarding efficacy, smokers treat e-cigarettes as valid alternatives to FDA-approved cessation aids. Research is needed to test the safety and efficacy of e-cigarettes as cessation aids.

http://www.ncbi.nlm.nih.gov/pubmed/23865700

Pilot Investigation of Changes in Readiness and Confidence to Quit Smoking After E-Cigarette Experimentation and 1 Week of Use

Theodore L. Wagener, PhD1, Ellen Meier, MS2, Jessica J. Hale, MS1, Elisha R. Oliver, MS1, Maggie L. Warner, BS1, Leslie M. Driskill, MS1, Stephen R. Gillaspy, PhD1, Michael B. Siegel, MD, MPH3 and Steven Foster, PhD4

# **Abstract**

Introduction: This study examined changes in smokers' readiness and confidence to quit smoking, smoking behavior, nicotine withdrawal symptoms, and tobacco product preference following electronic cigarette (EC) experimentation and 1 week of ad libitum use.

Methods: Current cigarette smokers, with no prior use of ECs and uninterested in quitting, completed 3 study phases: baseline assessment (N = 20), experimentation (N = 19), and ad

libitum use (N = 16). Baseline assessment consisted of completion of assessment measures and exhaled carbon monoxide measurements. Experimentation phases consisted of four, 75-min sessions in which participants completed assessment measures and sampled 3 EC brands and their own brand of cigarette (OBC). Ad libitum use included participants selecting and being provided their preferred EC brand from the experimentation phase to be used "as you want" for 1 week. Outcome measures included readiness and confidence to quit smoking, nicotine withdrawal symptoms, product preference/satisfaction, and smoking behavior items.

Results: Readiness and confidence to quit increased significantly during the experimentation period and continued to increase during ad libitum use. There were no significant differences in reported effectiveness in reducing smoking urges and cravings between OBC and EC though OBC were rated as more enjoyable and satisfying. During ad libitum use, regular cigarette smoking decreased by approximately 44% from baseline levels with overall tobacco use (EC + OBC) remaining the same.

Conclusions: Among a small convenience sample of unmotivated cigarette smokers, EC experimentation and 1 week of ad libitum use increased readiness and confidence to quit regular cigarettes and reduced regular cigarette smoking.

http://ntr.oxfordjournals.org/content/16/1/108.short

EffiCiency and Safety of an eLectronic cigAreTte (ECLAT) as Tobacco Cigarettes Substitute: A Prospective 12-Month Randomized Control Design Study

Pasquale Caponnetto, Davide Campagna, Fabio Cibella, Jaymin B. Morjaria, Massimo Caruso, Cristina Russo, Riccardo Polosa

**Abstract** 

Background

Electronic cigarettes (e-cigarettes) are becoming increasingly popular with smokers worldwide. Users report buying them to help quit smoking, to reduce cigarette consumption, to relieve tobacco withdrawal symptoms, and to continue having a 'smoking' experience, but with reduced health risks. Research on e-cigarettes is urgently needed in order to ensure that the decisions of regulators, healthcare providers and consumers are based on science.

Methods ECLAT is a prospective 12-month randomized, controlled trial that evaluates smoking reduction/abstinence in 300 smokers not intending to quit experimenting two different nicotine strengths of a popular e-cigarette model ('Categoria'; Arbi Group Srl, Italy) compared to its non-nicotine choice. GroupA (n=100) received 7.2 mg nicotine cartridges for 12 weeks; GroupB (n=100), a 6-week 7.2 mg nicotine cartridges followed by a further 6-week 5.4 mg nicotine cartridges; GroupC (n=100) received no-nicotine cartridges for 12 weeks. The study consisted of nine visits during which cig/day use and exhaled carbon monoxide (eCO) levels were measured. Smoking reduction and abstinence rates were calculated. Adverse events and product preferences were also reviewed.

### Results

Declines in cig/day use and eCO levels were observed at each study visits in all three study groups (p<0.001 vs baseline), with no consistent differences among study groups. Smoking reduction was documented in 22.3% and 10.3% at week-12 and week-52 respectively. Complete abstinence from tobacco smoking was documented in 10.7% and 8.7% at week-12 and week-52 respectively. A substantial decrease in adverse events from baseline was observed and withdrawal symptoms were infrequently reported during the study. Participants' perception and acceptance of the product under investigation was satisfactory.

#### Conclusion

In smokers not intending to quit, the use of e-cigarettes, with or without nicotine, decreased cigarette consumption and elicited enduring tobacco abstinence without causing significant side effects.

# http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0066317

'Vaping' profiles and preferences: an online survey of electronic cigarette users

Lynne Dawkins\*, John Turner, Amanda Roberts and Kirstie Soar

# **Abstract**

To characterize e-cigarette use, users and effects in a sample of Electronic Cigarette Company (TECC) and Totally Wicked E-Liquid (TWEL) users.

# Design and setting

Online survey hosted at the University of East London with links from TECC/TWEL websites from September 2011 to May 2012.

# Measurements

Online questionnaire.

#### **Participants**

One thousand three hundred and forty-seven respondents from 33 countries (72% European), mean age 43 years, 70% male, 96% Causacian, 44% educated to degree level or above.

# **Findings**

Seventy-four percent of participants reported not smoking for at least a few weeks since using the e-cigarette and 70% reported reduced urge to smoke. Seventy-two percent of participants used a 'tank' system, most commonly, the eGo-C (23%). Mean duration of use was 10 months. Only 1% reported exclusive use of non-nicotine (0 mg) containing liquid. E-cigarettes were generally considered to be satisfying to use; elicit few side effects; be healthier than smoking; improve cough/breathing; and be associated with low levels of craving. Among ex-smokers, 'time to first vape' was significantly longer than 'time to first cigarette' (t1104 = 11.16,

P < 0.001) suggesting a lower level of dependence to e-cigarettes. Ex-smokers reported significantly greater reduction in craving than current smokers ( $\chi 21 = 133.66$ , P < 0.0007) although few other differences emerged between these groups. Compared with males, females opted more for chocolate/sweet flavours ( $\chi 21 = 16.16$ , P < 0.001) and liked the e-cigarette because it resembles a cigarette ( $\chi 23 = 42.65$ , P < 0.001).

#### Conclusions

E-cigarettes are used primarily for smoking cessation, but for a longer duration than nicotine replacement therapy, and users believe them to be safer than smoking.

http://onlinelibrary.wiley.com/doi/10.1111/add.12150/abstract

Electronic cigarettes (e-cigs): views of aficionados and clinical/public health perspectives

J. Foulds, S. Veldheer and A. Berg

Background: Electronic cigarettes (e-cigs) have experienced a rapid growth in popularity but little is known about how they are used.

# **Abstract**

Aim: The aim of this study was to identify the e-cig products used by experienced e-cig users, their pattern of e-cig use and the impact on tobacco use.

Method: Face-to-face survey of 104 experienced e-cig users.

Results: Of all the e-cig users, 78% had not used any tobacco in the prior 30 days. They had previously smoked an average of 25 cigarettes per day, and had tried to quit smoking an average of nine times before they started using e-cigs. Two-thirds had previously tried to quit smoking using an FDA-approved smoking cessation medication. The majority of the sample had used e-cigs daily for at least a year. Three quarters started using e-cigs with the intention of quitting smoking and almost all felt that the e-cig had helped them to succeed in quitting

smoking. Two-thirds used e-cig liquid with a medium to high concentration of nicotine (13 mg +). Only 8% were using the most widely sold types of cigarette-sized e-cigs that are typically powered by a single 3.7 volt battery. Instead most used e-cigs designed to enable the atomizer to more consistently achieve a hotter more intense vapour.

Conclusion: Until we have more evidence on the safety and efficacy of e-cigs for smoking cessation, smokers should be advised to use proven treatments (e.g. counselling and FDA-approved medicines). However, for those who have successfully switched to e-cigs, the priority should be staying off cigarettes, rather than quitting e-cigs.

http://onlinelibrary.wiley.com/doi/10.1111/j.1742-1241.2011.02751.x/abstract

Research on reducing tobacco use

Research on vaping safety

Formaldehyde

Other information

# Other Information

Resource

Date

Author

Key points

California State University Apr 2015 Chemistry Professor: 'No

Scientific Reason to Restrict Vaping'

Friedman quoting Dr **Nichols** 

"The 'scientific' basis on which vaping has so far been restricted, frankly, simply doesn't exist. Restricting the use of vaping devices results only in more people continuing to smoke tobacco rather than turning to vaping to help stop a deadly habit that kills almost half a million people in America alone each year."

Web link with link to radio interview: http://bradblog.com/?p=11103

E-Cigarettes Poised to Save Medicaid Billions

Mar 2015 State Budget Solutions: Moody

"The game-changing potential for dramatic harm reduction by current smokers using e-cigs will flow directly into lower healthcare costs dealing with the morbidity and mortality stemming from smoking combustible cigarettes. These benefits will particularly impact the Medicaid system where the prevalence of cigarette smoking is twice that of the general public."

Web link: http://www.statebudgetsolutions.org/publications/detail/e-cigarettes-poised-to-save-medicaid-billions

Chemical analysis of Natural Extract of Tobacco (NET) liquids

Mar 2015 Farsalinos et al Some electronic cigarette (EC) liquids of tobacco flavour contain extracts of cured tobacco leaves produced by a process of solvent extraction and steeping.

21 samples, 11 Natural Extract of Tobacco (NET) liquids and 10 conventional eliquids were analysed:

- NET liquids contained higher levels of phenols and nitrates, but lower levels of acetaldehyde compared to conventional EC liquids.
- The lower levels of tobacco-derived toxins found in NET liquids compared to tobacco products indicate that the extraction process used to make these products did not transfer a significant amount of toxins to the NET.
- Overall, all EC liquids contained far lower (by 2-3 orders of magnitude) levels of the tobacco-derived toxins compared to tobacco products.

Web link: http://www.mdpi.com/1660-4601/12/4/3439

Alarmist survey on teenage vaping misses the point

Mar 2015 Bates (The Counterfactual)

The BBC reported on a new study, Associations between e-cigarette access and smoking and drinking behaviours in teenagers, that 'showed one in five had tried or bought e-cigarettes'.

Examination of key issues for assessing the implications of the survey, and including expert responses.

http://www.clivebates.com/?p=2961

Briefing on e-cigarettes for policy makers Version Feb 2015 The

Counterfactual:

Clive Bates

Background

The public health case - tobacco harm reduction

What are critics concerned about?

Regulatory issues.

PDF: http://www.clivebates.com/documents/vapebriefing.pdf

Cigarette revenues down. Jan 2015 Rafool (State A revenue quagmire.

Leg Magazine)

Sales of regular cigarettes decreased by 30 percent from 2004, according to the Centers for Disease Control and Prevention, and that brought down state revenues too, because cigarettes are among the highest taxed products in the country.

Tax policy scholars argue against taxing electronic cigarettes because vaping may reduce the number of regular tobacco users by providing a satisfying alternative. If true, vaping provides a net benefit for society, which should not be discouraged by taxing e-cigarettes.

Web link: http://www.ncsl.org/research/fiscal-policy/vaporized.aspx

Massive drop in tobacco Dec 2014 National use among teens

Institute on Drug Abuse "Daily cigarette smoking has decreased markedly over the past five years (almost 50 percent) across all grades.

'We are concerned about the levels of e-cigarette use among teens that we are seeing' said Lloyd Johnston, principal investigator."

Web link: http://www.drugabuse.gov/news-events/news-releases/2014/12/teen-prescription-opioid-abuse-cigarette-alcohol-usetrends-down

E-cigarette gateway claim Dec 2014 Reason.org:

Jacob Sullum

"Vaping rises to record highs, smoking falls to record lows, and activists insist

'e-cigarettes are a gateway to smoking'.

The crucial question, in assessing the 'public health' impact of ecigarettes, is whether they compete with tobacco cigarettes or somehow expand the market for them. The evidence so far clearly supports the former view."

Web link: http://reason.com/blog/2014/12/17/vaping-rises-to-record-highs-smoking-fal

E-cigarettes have not been a gateway to traditional smoking -ONS

Nov 2014 UK Office for

National Statistics via Guardian

Estimates 2.1m people in Great Britain currently using e-cigarettes E-cigarettes are used almost exclusively by smokers and ex-smokers. Only 0.14% of non-smokers use e-cigarettes.

Results back up the findings of a YouGov Survey showing half of those using e-cigarettes viewed it as a way to transition off smoking completely

Web link: http://www.theguardian.com/news/datablog/2014/nov/25/e-cigarettes-not-gateway-traditional-smoking-great-britain

Change in Tobacco Consumption in Australia 2014

June

Fairfax Media via Aust Bureau of **Statistics** 

Rollover interactive chart, demonstrating a rise in consumption when "plain packaging" was introduced. And a rapid decline between 2013 and 2014 when taxes were highest and vaping became popular.

Web link: http://cf.datawrapper.de/d1yM2/5/

French ruling treating ecigarettes as tobacco products

Mar 2014 Addiction:

Franchitto

"French judges decided to assimilate e-cigarettes to tobacco products because they resembled manufactured cigarettes. They focused only on the commercial and fiscal aspects of the law by citing the Tax Code, and also justified their ruling through the provisions of the French Public Health Code, which prohibits advertising for such products in order to protect public health. However, the judges ignored both scientific evidence and scientific uncertainties concerning the overall public health benefit of ecigarettes"

Web link: http://onlinelibrary.wiley.com/doi/10.1111/add.12521/full

Memo on Pharma lobbying

Feb 2014 Bloomberg news: Kitamura

GlaxoSmithKline Plc (GSK) is pushing for more stringent regulation of electronic cigarettes, which compete with its Nicorette gum and other smoking cessation products, according to e-mails from a company executive.

J&J, which markets the Nicorette line of products in all markets outside the US, is also "strongly in favor of" regulating all non-tobacco nicotine products, including e-cigarettes, as medicines.

Web link: http://mobile.bloomberg.com/news/2014-02-19/glaxo-memo-shows-drug-industry-lobbying-on-e-cigarettes.html

Big Drug's Nicotine War

July 2001 Hamilton, Forces Intl Nicotine is a highly profitable drug with enormous therapeutic potential. While the drug itself can't be patented, the means of delivery can. This paper chronicles how the large pharmaceuticals have colluded with government agencies and NGOs to wrest control of the drug from Big Tobacco, to replace one means of drug distribution with a range of others.

Web link (pdf): http://www.forces.org/evidence/pharma/pdf/fullwork.pdf

Use of E-cigarettes by young is still rare

Sep 2013 ASH UK

"ASH supports the introduction of an age of sale of 18 for electronic cigarettes and stricter controls on how they're advertised as a precautionary measure to prevent these products being promoted to children. However, our survey results should reassure the public that electronic cigarettes are not currently widely used by young people, nor are they interested in taking electronic cigarettes up. The small increases in use that have occurred over the last year are almost entirely among children who smoke or have smoked."

Web link: http://www.ash.org.uk/media-room/press-releases/:new-survey-finds-regular-use-of-electronic-cigarettes-by-children-still-rare

Pharmaceutical NRT doesn't work in the real world

Jan 2012 BMJ: Alpert et al

"This study finds that persons who have quit smoking relapsed at equivalent rates, whether or not they used NRT to help them in their quit attempts."

Quit smoking services continue to refer the public to these products despite the lack of real world evidence that they work.

Web links: http://theconversation.com/nicotine-replacement-therapy-isnt-all-its-cracked-up-to-be-12153 http://tobaccocontrol.bmj.com/content/22/1/32.abstract

Flavour variability and ecig use

Dec 2013 Farsalinos

"(Flavours) are important for vapers' efforts to stay off cigarettes and they are not targeting youngsters (as accused by the news media and several political groups). Considering the fact that adoption of e-cigarettes by youngsters is minimal (and mostly observed in smokers), any regulation that would restrict flavors variability would be inappropriate."

Web link; http://www.ecigarette-research.com/web/index.php/research/2013/145-e-cigarette-flavors

Australia 'Plain' Packaging, no effect on sales Nov 2014 ANU study cited by Snowdon (blog)

"Despite our econometric efforts, the data refused to yield any indication this policy has been successful; there is no empirical evidence to support the notion that the plain packaging policy has resulted in lower household expenditure on tobacco than there otherwise would have been. There is some faint evidence to suggest, ceteris paribus, household expenditure on tobacco increased."

Web link: http://velvetgloveironfist.blogspot.se/2014/11/plain-packaging-had-no-effect-on-sales.html?m=1

Environmental Tobacco Smoke and Lung Cancer Jul 1998 Journal of the Natl Cancer

Institute: Boffetta et al Our results indicate no association between childhood exposure to environmental tobacco smoke (ETS) and lung cancer risk. We did find weak evidence of a dose-response relationship between risk of lung cancer and exposure to spousal and workplace ETS. There was no detectable risk after cessation of exposure."

Web link: http://jnci.oxfordjournals.org/content/90/19/1440

Electronic cigarettes: getting the science right and communicating it effectively 2013

Addiction: West and Babor "It is worth highlighting the ways in which science is being misused so that readers can be better placed to evaluate the messages:

- · Failure to quantify
- · Failure to account for confounding and reverse causality
- Selective reporting
- Misrepresentation of outcome measures
- · Double standards in what is accepted as evidence
- · Discrediting the source"

Web link: http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1360-0443/homepage/electronic\_cigarettes.htm

Comments

E-cigarettes: an evidence update A report commissioned by Public Health England Authors: McNeill A, Brose LS, Calder R, Hitchman SC Institute of Psychiatry, Psychology & Neuroscience, National Addiction Centre, King's College London UK Centre for Tobacco & Alcohol Studies Hajek P, McRobbie H (Chapters 9 and 10) Wolfson Institute of Preventive Medicine, Barts and The London School of Medicine and Dentistry Queen Mary, University of London UK Centre for Tobacco & Alcohol Studies

# **Executive Summary**

Following two previous reports produced for Public Health England (PHE) on ecigarettes (EC) in 2014, this report updates and expands on the evidence of the implications of EC for public health. It covers the EC policy framework, the prevalence of EC use, knowledge and attitudes towards EC, impact of EC use on smoking behaviour, as well as examining recent safety issues and nicotine content, emissions and delivery. Two literature reviews were carried out to update the evidence base since the 2014 reports and recent survey data from England were assessed. EC use battery power to heat an element to disperse a solution of propylene glycol or glycerine, water, flavouring and usually nicotine, resulting in an aerosol that can be inhaled by the user (commonly termed vapour). EC do not contain tobacco, do not create smoke and do not rely on combustion. There is substantial heterogeneity between different types of EC on the market (such as cigalikes and tank models). Acknowledging that the evidence base on overall and relative risks of EC in comparison with smoking was still developing, experts recently identified them as having around 4% of the relative harm of cigarettes overall (including social harm) and 5% of the harm to users. In England, EC first appeared on the market within the last 10 years and around 5% of the population report currently using them, the vast majority of these smokers or recent ex-smokers. Whilst there is some experimentation among never smokers, regular use among never smokers is rare. Cigarette smoking among youth and adults has continued to decline and there is no current evidence in England that EC are renormalising smoking or increasing smoking uptake. Instead, the evidence reviewed in this report point in the direction of an association between greater uptake of EC and reduced smoking, with emerging evidence that EC can be effective cessation and reduction aids. Regulations have changed little in England since the previous PHE reports with EC being currently governed by general product safety regulations which do not require products to be tested before being put on the market. However, advertising of EC is now governed by a voluntary agreement and measures are being introduced to protect children from accessing EC from retailers. Manufacturers can apply for a medicinal licence through the Medicines and Healthcare products Regulatory Agency (MHRA) and from 2016, any EC not licensed by the MHRA will be governed by the revised European Union Tobacco Products Directive (TPD).

https://www.gov.uk/government/uploads/system/uploads/attachment data/file/457102/Ecigarettes an evidence update A report commissioned by Public Health England FINAL.pdf

Electronic cigarette use and harm reversal: emerging evidence in the lung Riccardo Polosa

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UOC di Medicina Interna e d'Urgenza, Edificio 4, Piano 3, AOU "Policlinico-V. Emanuele", Via S. Sofia 78, Catania, 95123, Italy BMC Medicine 2015, 13:54 doi:10.1186/s12916-015-0298-3 The electronic version of this article is the complete one and can be found online at:http://www.biomedcentral.com/1741-7015/13/54

# Abstract

Electronic cigarettes (ECs) have been rapidly gaining ground on conventional cigarettes due to their efficiency in ceasing or reducing tobacco consumption, competitive prices, and the perception of them being a much less harmful smoking alternative. Direct confirmation that long-term EC use leads to reductions in smoking-related diseases is not available and it will take a few decades before the tobacco harm reduction potential of this products is firmly established. Nonetheless, it is feasible to detect early changes in airway function and respiratory symptoms in smokers switching to e-vapor. Acute investigations do not appear to support negative respiratory health outcomes in EC users and initial findings from long-term studies are supportive of a beneficial effect of EC use in relation to respiratory outcomes. The emerging evidence that EC use can reverse harm from tobacco smoking should be taken into consideration by regulatory authorities seeking to adopt proportional measures for the e-vapor category.

http://www.biomedcentral.com/1741-7015/13/54

Regulatory Toxicology and Pharmacology Volume 70, Issue 3, December 2014, Pages 704–710

Comparison of select analytes in aerosol from e-cigarettes with smoke from conventional cigarettes and with ambient air
Rana Tayyarah, , Gerald A. Long

# Highlights

The e-cigarettes contained and delivered mostly glycerin and/or PG and water.

Aerosol nicotine content was 85% lower than the cigarette smoke nicotine.

The levels of HPHCs in aerosol were consistent with the air blanks ( $<2 \mu g/puff$ ).

Mainstream cigarette smoke HPHCs (  $3000 \, \mu g/puff$ ) were 1500 times higher than ecigarette HPHCs.

No significant contribution of tested HPHC classes was found for the e-cigarettes.

#### Abstract

Leading commercial electronic cigarettes were tested to determine bulk composition. The e-cigarettes and conventional cigarettes were evaluated using machine-puffing to compare nicotine delivery and relative yields of chemical constituents. The e-liquids tested were found to contain humectants, glycerin and/or propylene glycol, ( 75% content); water (<20%); nicotine (approximately 2%); and flavor (<10%). The aerosol collected mass (ACM) of the e-cigarette samples was similar in composition to the eliquids. Aerosol nicotine for the e-cigarette samples was 85% lower than nicotine yield for the conventional cigarettes. Analysis of the smoke from conventional cigarettes showed that the mainstream cigarette smoke delivered approximately 1500 times more harmful and potentially harmful constituents (HPHCs) tested when compared to ecigarette aerosol or to puffing room air. The deliveries of HPHCs tested for these ecigarette products were similar to the study air blanks rather than to deliveries from conventional cigarettes; no significant contribution of cigarette smoke HPHCs from any of the compound classes tested was found for the e-cigarettes. Thus, the results of this study support previous researchers' discussion of e-cigarette products' potential for reduced exposure compared to cigarette smoke.

http://www.sciencedirect.com/science/article/pii/S0273230014002505

Addiction. 2014 Nov;109(11):1801-10. doi: 10.1111/add.12659. Epub 2014 Jul 31. Electronic cigarettes: review of use, content, safety, effects on smokers and potential for harm and benefit.

<u>Hajek P1</u>, <u>Etter JF</u>, <u>Benowitz N</u>, <u>Eissenberg T</u>, <u>McRobbie H</u>. <u>Author information</u>

#### Abstract

#### AIMS:

We reviewed available research on the use, content and safety of electronic cigarettes (EC), and on their effects on users, to assess their potential for harm or benefit and to extract evidence that can guide future policy.

## METHODS:

Studies were identified by systematic database searches and screening references to February 2014.

# **RESULTS:**

EC aerosol can contain some of the toxicants present in tobacco smoke, but at levels which are much lower. Long-term health effects of EC use are unknown but compared with cigarettes, EC are likely to be much less, if at all, harmful to users or bystanders. EC are increasingly popular among smokers, but to date there is no evidence of regular use by never-smokers or by non-smoking children. EC enable some users to reduce or quit smoking.

#### CONCLUSIONS:

Allowing EC to compete with cigarettes in the market-place might decrease smoking-related morbidity and mortality. Regulating EC as strictly as cigarettes, or even more strictly as some regulators propose, is not warranted on current evidence. Health professionals may consider advising smokers unable or unwilling to quit through other routes to switch to EC as a safer alternative to smoking and a possible pathway to complete cessation of nicotine use.

http://www.ncbi.nlm.nih.gov/pubmed/?term=Electronic+cigarettes%3A+review+of+use%2C+content%2C+safety%2C+effects+on+smokers+and+potential+for+harm+and+benefit

Int. J. Environ. Res. Public Health 2014, 11(11), 11325-11347;

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Article

Comparative In Vitro Toxicity Profile of Electronic and Tobacco Cigarettes, Smokeless Tobacco and Nicotine Replacement Therapy Products: E-Liquids, Extracts and Collected Aerosols

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(This article belongs to the Special Issue <u>Electronic Cigarettes as a Tool in Tobacco</u> Harm Reduction)

View Full-Text | Download PDF [683 KB, 4 November 2014; original version 30

October 2014] | Browse Figures

#### Abstract

The use of electronic cigarettes (e-cigs) continues to increase worldwide in parallel with accumulating information on their potential toxicity and safety. In this study, an in vitro battery of established assays was used to examine the cytotoxicity, mutagenicity, genotoxicity and inflammatory responses of certain commercial e-cigs and compared to tobacco burning cigarettes, smokeless tobacco (SLT) products and a nicotine replacement therapy (NRT) product. The toxicity evaluation was performed on e-liquids and pad-collected aerosols of e-cigs, pad-collected smoke condensates of tobacco cigarettes and extracts of SLT and NRT products. In all assays, exposures with e-cig liquids and collected aerosols, at the doses tested, showed no significant activity when compared to tobacco burning cigarettes. Results for the e-cigs, with and without nicotine in two evaluated flavor variants, were very similar in all assays, indicating that the presence of nicotine and flavors, at the levels tested, did not induce any cytotoxic, genotoxic or inflammatory effects. The present findings indicate that neither the e-cig liquids and collected aerosols, nor the extracts of the SLT and NRT products produce any meaningful toxic effects in four widely-appliedin vitro test systems, in which the conventional cigarette smoke preparations, at comparable exposures, are markedly cytotoxic and genotoxic.

http://www.mdpi.com/1660-4601/11/11/11325

# Regulatory Toxicology and Pharmacology Volume 71, Issue 1, February 2015, Pages 24–34

Effects of using electronic cigarettes on nicotine delivery and cardiovascular function in comparison with regular cigarettes

X. Sherwin Yan, , Carl D'Ruiz

# Highlights

E-cig users showed significantly lower nicotine C90 than Marlboro® cigarette users.

Use of Marlboro® cigs led to significant elevation of blood pressure and heart rate.

Use of e-cigs showed less magnitude of increase of BP and HR than cigarette smoking.

Use of Marlboro® cigs significantly increased the exhaled CO 8+ times above baseline.

# **Abstract**

The development of electronic cigarettes (e-cigs) has the potential to offer a less harmful alternative for tobacco users. This clinical study was designed to characterize ecig users' exposure to nicotine, and to investigate the acute effects of e-cigs on the hemodynamic measurements (blood pressure and heart rate) in comparison with the effects of regular smoking. Five e-cigs and one Marlboro® cigarette were randomized for twenty-three participants under two exposure scenarios from Day 1 to Day 11: half-hour controlled administration and one hour ad lib use. The nicotine plasma concentrations after 1.5 h of product use (C90) were significantly lower in the users of e-cigs than of Marlboro® cigarettes. The combination of glycerin and propylene glycol as the vehicle facilitated delivery of more nicotine than glycerin alone. The heart rate, systolic and diastolic blood pressure were significantly elevated after use of Marlboro® cigarettes, but the elevation was less after use of most of the e-cigs. Use of e-cigs had no impact on the exhaled CO levels, whereas the Marlboro® cigarette significantly increased the exhaled CO more than 8 times above the baseline. In conclusion, e-cigs could be a less harmful alternative for tobacco users.

http://www.sciencedirect.com/science/article/pii/S0273230014002797

Comparison of Select Analytes in Exhaled Aerosol from E-Cigarettes with Exhaled Smoke from a Conventional Cigarette and Exhaled Breaths

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Lorillard Tobacco Company, P.O. Box 21688, Greensboro, NC 27420, USA Received: 21 August 2014 / Revised: 14 October 2014 / Accepted: 16 October 2014 /

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(This article belongs to the Special Issue Electronic Cigarettes as a Tool in Tobacco

Harm Reduction)

View Full-Text | Download PDF [519 KB, uploaded 27 October 2014] | Browse

Figures

# Abstract

Exhaled aerosols were collected following the use of two leading U.S. commercial electronic cigarettes (e-cigarettes) and a conventional cigarette by human subjects and analyzed for phenolics, carbonyls, water, glycerin and nicotine using a vacuum-assisted filter pad capture system. Exhaled breath blanks were determined for each subject prior to each product use and aerosol collection session. Distribution and mass balance of exhaled e-cigarette aerosol composition was greater than 99.9% water and glycerin, and a small amount (<0.06%) of nicotine. Total phenolic content in exhaled e-cigarette aerosol was not distinguishable from exhaled breath blanks, while total phenolics in exhaled cigarette smoke were significantly greater than in exhaled e-cigarette aerosol and exhaled breaths, averaging 66 µg/session (range 36 to 117 µg/session). The total carbonyls in exhaled e-cigarette aerosols were also not distinguishable from exhaled breaths or room air blanks. Total carbonyls in exhaled cigarette smoke was significantly greater than in exhaled e-cigarette aerosols, exhaled breath and room air blanks, averaging 242 µg/session (range 136 to 352 µg/session). These results indicate that exhaled e-cigarette aerosol does not increase bystander exposure for phenolics and carbonyls above the levels observed in exhaled breaths of air.

http://www.mdpi.com/1660-4601/11/11/1177

Particulate metals and organic compounds from electronic and tobacco-containing cigarettes: comparison of emission rates and secondhand exposure

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Environ. Sci.: Processes Impacts, 2014,16, 2259-2267

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Received 27 Jul 2014, Accepted 21 Aug 2014 First published online 22 Aug 2014

#### Abstract

In recent years, electronic cigarettes have gained increasing popularity as alternatives to normal (tobacco-containing) cigarettes. In the present study, particles generated by ecigarettes and normal cigarettes have been analyzed and the degree of exposure to different chemical agents and their emission rates were quantified. Despite the 10-fold decrease in the total exposure to particulate elements in e-cigarettes compared to normal cigarettes, specific metals (e.g. Ni and Ag) still displayed a higher emission rate from e-cigarettes. Further analysis indicated that the contribution of e-liquid to the emission of these metals is rather minimal, implying that they likely originate from other components of the e-cigarette device or other indoor sources. Organic species had lower emission rates during e-cigarette consumption compared to normal cigarettes. Of particular note was the non-detectable emission of polycyclic aromatic hydrocarbons (PAHs) from e-cigarettes, while substantial emission of these species was observed from normal cigarettes. Overall, with the exception of Ni, Zn, and Ag, the consumption of e-cigarettes resulted in a remarkable decrease in secondhand exposure to all metals and organic compounds. Implementing quality control protocols on the manufacture of e-cigarettes would further minimize the emission of metals from these devices and improve their safety and associated health effects.

http://pubs.rsc.org/en/content/articlelanding/2014/em/c4em00415a#!divAbstract

CORRESPONDENCE
Nicotine Poisoning in an Infant
N Engl J Med 2014; 370:2249-2250June 5, 2014
DOI: 10.1056/NEJMc140384

# To the Editor:

Reports to U.S. poison control centers of possible nicotine toxicity tripled from 2012 to 2013.1,2 Although nicotine toxicity is not a new phenomenon, the emergence of electronic cigarettes ("e-cigarettes") has spawned a market for highly concentrated liquid nicotine. This phenomenon has resulted in unprecedented access to potentially toxic doses of nicotine and other harmful compounds in the home. We report a case of a child who was poisoned by e-cigarette refill liquid ("e-liquid"). Vomiting, tachycardia, grunting respirations, and truncal ataxia developed in a 10month-old boy after he ingested a "small" amount of e-liquid nicotine. The vaping (or "vape") shop that compounded the product reported that it contained a nicotine concentration of 1.8% (18 mg per milliliter) and unknown concentrations of oil of wintergreen (methyl salicylate), glycerin, and propylene glycol. Multiple toxidromes that could have been associated with ingestion of this type of product include cholinergic crisis and salicylism. Low doses of nicotine frequently have stimulant effects (e.g., tachycardia). Vomiting is common with enteral exposures. Signs of central nervous system toxicity include ataxia and seizures. As doses increase, loss of nicotinic receptor specificity may occur and result in signs of muscarinic cholinergic toxicity, including extreme secretions and gastrointestinal disturbance. The highest levels of poisoning can result in neuromuscular blockade, respiratory failure, and death. Small ingestions could be deadly. With an estimated median lethal dose between 1 and 13 mg per kilogram of body weight, 1 teaspoon (5 ml) of a 1.8% nicotine solution could be lethal to a 90-kg person.3,4

Fortunately, our patient's levels of consciousness, hemoglobin oxygen, and serum salicylate, as well as findings on chest radiography and his basic metabolic profile, were all normal. The boy did not require antidote therapy (usually atropine or scopolamine to combat cholinergic activity) and recovered baseline health 6 hours after ingesting the poison.

The Food and Drug Administration does not currently regulate nontherapeutic nicotine; this raises concern that in the ballooning unregulated liquid nicotine market there may be variability in nicotine dosing and introduction of unintended toxic ingredients. Lack of regulatory oversight has resulted in inconsistent labeling, insufficient or nonexistent child protective packaging, and product design and flavoring that may encourage children to explore and ingest these products. Figure 1

Three Examples of Over-the-Counter Liquid Nicotine Products. shows labeling that contains suggestions of edible ingredients ("lemonade"), visually appealing cartoons, and handwritten labels of uncertain reliability. With the growing use of e-cigarettes, physicians need to be alert for nicotine poisoning. They also need to educate patients and parents about this danger and advocate for

measures that will help prevent potentially fatal liquid nicotine poisoning of infants and young children.

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#### Abstract

Significance Electronic cigarettes, also known as e-cigarettes, are devices designed to imitate regular cigarettes and deliver nicotine via inhalation without combusting tobacco. They are purported to deliver nicotine without other toxicants and to be a safer alternative to regular cigarettes. However, little toxicity testing has been performed to evaluate the chemical nature of vapour generated from e-cigarettes. The aim of this study was to screen e-cigarette vapours for content of four groups of potentially toxic and carcinogenic compounds: carbonyls, volatile organic compounds, nitrosamines and heavy metals.

Materials and methods Vapours were generated from 12 brands of e-cigarettes and the reference product, the medicinal nicotine inhaler, in controlled conditions using a modified smoking machine. The selected toxic compounds were extracted from vapours into a solid or liquid phase and analysed with chromatographic and spectroscopy

methods.

Results We found that the e-cigarette vapours contained some toxic substances. The levels of the toxicants were 9–450 times lower than in cigarette smoke and were, in many cases, comparable with trace amounts found in the reference product.

Conclusions Our findings are consistent with the idea that substituting tobacco cigarettes with e-cigarettes may substantially reduce exposure to selected tobacco-specific toxicants. E-cigarettes as a harm reduction strategy among smokers unwilling to quit, warrants further study. (To view this abstract in Polish and German, please see the supplementary files online.)

http://tobaccocontrol.bmj.com/content/early/2013/03/05/tobaccocontrol-2012-050859.short

Inhalation Toxicology: International Forum for Respiratory Research Volume 25, Issue 6, 2013

Research Article

Cytotoxicity evaluation of electronic cigarette vapor extract on cultured mammalian fibroblasts (ClearStream-LIFE): comparison with tobacco cigarette smoke extract

DOI:10.3109/08958378.2013.793439

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pages 354-361

Publishing models and article dates explained

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Abstract

Context: Electronic cigarettes (ECs) are used as alternatives to smoking; however, data on their cytotoxic potential are scarce.

Objective: To evaluate the cytotoxic potential of 21 EC liquids compared to the effects of

cigarette smoke (CS).

Methods: Cytotoxicity was evaluated according to UNI EN ISO 10993-5 standard. By activating an EC device, 200 mg of liquid was evaporated and was extracted in 20 ml of culture medium. CS extract from one cigarette was also produced. The extracts, undiluted (100%) and in five dilutions (50%, 25%, 12.5%, 6.25% and 3.125%), were applied to cultured murine fibroblasts (3T3), and viability was measured after 24-hour incubation by 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide assay. Viability of less than 70% was considered cytotoxic.

Results: CS extract showed cytotoxic effects at extract concentrations above 12.5% (viability:  $89.1\pm3.5\%$  at 3.125%,  $77.8\pm1.8\%$  at 6.25%,  $72.8\pm9.7\%$  at 12.5%,  $5.9\pm0.9\%$  at 25%,  $9.4\pm5.3\%$  at 50% and  $5.7\pm0.7\%$  at 100% extract concentration). Range of fibroblast viability for EC vapor extracts was 88.5-117.8% at 3.125%, 86.4-115.3% at 6.25%, 85.8-111.7% at 12.5%, 78.1-106.2% at 25%, 79.0-103.7% at 50% and 51.0-102.2% at 100% extract concentration. One vapor extract was cytotoxic at 100% extract concentration only (viability:  $51.0\pm2.6\%$ ). However, even for that liquid, viability was 795% higher relative to CS extract.

Conclusions: This study indicates that EC vapor is significantly less cytotoxic compared tobacco CS. These results should be validated by clinical studies.

http://www.tandfonline.com/doi/abs/10.3109/08958378.2013.793439

Metal and Silicate Particles Including Nanoparticles Are Present in Electronic Cigarette Cartomizer Fluid and Aerosol

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- Amanda Villarreal,
- Krassimir Bozhilov.
- Sabrina Lin,
- Prue Talbot
- Published: March 20, 2013

# Abstract

# Background

Electronic cigarettes (EC) deliver aerosol by heating fluid containing nicotine. Cartomizer EC combine the fluid chamber and heating element in a single unit. Because EC do not burn tobacco, they may be safer than conventional cigarettes. Their use is rapidly increasing worldwide with little prior testing of their aerosol.

# Objectives

We tested the hypothesis that EC aerosol contains metals derived from various components in EC.

#### Methods

Cartomizer contents and aerosols were analyzed using light and electron microscopy, cytotoxicity testing, x-ray microanalysis, particle counting, and inductively coupled plasma optical emission spectrometry.

# Results

The filament, a nickel-chromium wire, was coupled to a thicker copper wire coated with silver. The silver coating was sometimes missing. Four tin solder joints attached the wires to each other and coupled the copper/silver wire to the air tube and mouthpiece. All cartomizers had evidence of use before packaging (burn spots on the fibers and electrophoretic movement of fluid in the fibers). Fibers in two cartomizers had green deposits that contained copper. Centrifugation of the fibers produced large pellets containing tin. Tin particles and tin whiskers were identified in cartridge fluid and outer fibers. Cartomizer fluid with tin particles was cytotoxic in assays using human pulmonary fibroblasts. The aerosol contained particles >1 µm comprised of tin, silver, iron, nickel, aluminum, and silicate and nanoparticles (<100 nm) of tin, chromium and nickel. The concentrations of nine of eleven elements in EC aerosol were higher than or equal to the corresponding concentrations in conventional cigarette smoke. Many of the elements identified in EC aerosol are known to cause respiratory distress and disease.

#### Conclusions

The presence of metal and silicate particles in cartomizer aerosol demonstrates the need for improved quality control in EC design and manufacture and studies on how EC aerosol impacts the health of users and bystanders.

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0057987
Int. J. Environ. Res. Public Health 2013, 10(6), 2500-2514; doi:10.3390/ijerph10062500
Article

Evaluation of Electronic Cigarette Use (Vaping) Topography and Estimation of Liquid Consumption: Implications for Research Protocol Standards Definition and for Public Health Authorities' Regulation

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## **Abstract**

Background: Although millions of people are using electronic cigarettes (ECs) and research on this topic has intensified in recent years, the pattern of EC use has not been systematically studied. Additionally, no comparative measure of exposure and nicotine delivery between EC and tobacco cigarette or nicotine replacement therapy (NRTs) has been established. This is important, especially in the context of the proposal for a new Tobacco Product Directive issued by the European Commission.Methods: A second generation EC device, consisting of a higher capacity battery and tank atomiser design compared to smaller cigarette-like batteries and cartomizers, and a 9 mg/mL nicotine-concentration liquid were used in this study. Eighty subjects were recruited; 45 experienced EC users and 35 smokers. EC users were video-recorded when using the device (ECIG group), while smokers were recorded when smoking (SM-S group) and when using the EC (SM-E group) in a randomized cross-over design. Puff, inhalation and exhalation duration were measured. Additionally, the amount of EC liquid consumed by experienced EC users was measured at 5 min (similar to the time needed to smoke one tobacco cigarette) and at 20 min (similar to the time needed for a nicotine inhaler to deliver 4 mg nicotine). Results: Puff duration was significantly higher in ECIG  $(4.2 \pm 0.7 \text{ s})$  compared to SM-S  $(2.1 \pm 0.4 \text{ s})$  and SM-E  $(2.3 \pm 0.5 \text{ s})$ , while inhalation time was lower (1.3  $\pm$  0.4, 2.1  $\pm$  0.4 and 2.1  $\pm$  0.4 respectively). No difference was observed in exhalation duration. EC users took 13 puffs and consumed 62 ± 16 mg liquid in 5 min; they took 43 puffs and consumed 219 ± 56 mg liquid in 20 min. Nicotine delivery was estimated at  $0.46 \pm 0.12$  mg after 5 min and  $1.63 \pm 0.41$  mg after 20 min of use. Therefore, 20.8 mg/mL and 23.8 mg/mL nicotine-containing liquids would deliver 1 mg of nicotine in 5 min and 4 mg nicotine in 20 min, respectively. Since the ISO method significantly underestimates nicotine delivery by tobacco cigarettes, it seems that liquids with even higher than 24 mg/mL nicotine concentration would be comparable to one tobacco cigarette. Conclusions: EC use topography is significantly different compared to smoking. Four-second puffs with 20-30 s interpuff interval should be used when assessing EC effects in laboratory experiments, provided that the equipment used does not get overheated. Based on the characteristics of the device used in this study, a 20 mg/mL nicotine concentration liquid would be needed in order to deliver nicotine at

amounts similar to the maximum allowable content of one tobacco cigarette (as measured by the ISO 3308 method). The results of this study do not support the statement of the European Commission Tobacco Product Directive that liquids with nicotine concentration of 4 mg/mL are comparable to NRTs in the amount of nicotine delivered to the user.

<u>Inhal Toxicol.</u> 2012 Oct;24(12):850-7. doi: 10.3109/08958378.2012.724728. Comparison of the effects of e-cigarette vapor and cigarette smoke on indoor air quality.

# McAuley TR1, Hopke PK, Zhao J, Babaian S. Author information

#### Abstract

## CONTEXT:

Electronic cigarettes (e-cigarettes) have earned considerable attention recently as an alternative to smoking tobacco, but uncertainties about their impact on health and indoor air quality have resulted in proposals for bans on indoor e-cigarette use.

## **OBJECTIVE:**

To assess potential health impacts relating to the use of e-cigarettes, a series of studies were conducted using e-cigarettes and standard tobacco cigarettes.

# **METHODS AND MATERIALS:**

Four different high nicotine e-liquids were vaporized in two sets of experiments by generic 2-piece e-cigarettes to collect emissions and assess indoor air concentrations of common tobacco smoke by products. Tobacco cigarette smoke tests were conducted for comparison.

## **RESULTS:**

Comparisons of pollutant concentrations were made between e-cigarette vapor and tobacco smoke samples. Pollutants included VOCs, carbonyls, PAHs, nicotine, TSNAs, and glycols. From these results, risk analyses were conducted based on dilution into a 40 m³ room and standard toxicological data. Non-cancer risk analysis revealed "No Significant Risk" of harm to human health for vapor samples from e-liquids (A-D). In contrast, for tobacco smoke most findings markedly exceeded risk limits indicating a condition of "Significant Risk" of harm to human health. With regard to cancer risk analysis, no vapor sample from e-liquids A-D exceeded the risk limit for either children or adults. The tobacco smoke sample approached the risk limits for adult exposure.

#### CONCLUSIONS:

For all byproducts measured, electronic cigarettes produce very small exposures relative to tobacco cigarettes. The study indicates no apparent risk to human health from e-cigarette emissions based on the compounds analyzed.

http://www.ncbi.nlm.nih.gov/pubmed/23033998

Safety Report on the Ruyan® e-cigarette Cartridge and Inhaled Aerosol Dr Murray Laugesen QSO, MBChB, FAFPHM, FRCS, Dip Obst

Health New Zealand Ltd Christchurch, New Zealand. <u>www.healthnz.co.nz</u> 30 October 2008

# Summary

Aim. This report aims to assist regulators in initial assessment of the safety of the Ruyan® e-cigarette and its cartridges, and the possible risks and benefits from permitting its use.

Method. Health New Zealand Ltd contracted with seven leading government, university and commercial laboratories in New Zealand and Canada to independently perform various tests on the Ruyan cigarette's nicotine refill cartridge.

Findings. Ruyan® e-cigarette is designed to be a safe alternative to smoking. The various test results confirm this is the case. It is very safe relative to cigarettes, and also safe in absolute terms on all measurements we have applied. Using micro-electronics it vaporizes, separately for each puff, very small quantities of nicotine dissolved in propylene glycol, two small well-known molecules with excellent safety profiles, – into a fine aerosol. Each puff contains one third to one half the nicotine in a tobacco cigarette's puff. The cartridge liquid is tobacco-free and no combustion occurs.

Competency. The author has authored or co-authored over 30 research papers and reports in national and international scientific medical journals since 1995, on smoking, and latterly on testing of cigarettes and cigarette substitutes. <a href="https://www.healthnz.co.nz/Publicnsall.htm">www.healthnz.co.nz/Publicnsall.htm</a>

Financial disclosure. This report is funded by Ruyan. Disclaimer. Apart from research Health New Zealand derives no financial benefit from Ruyan.

Limitation. Unless the contrary is stated, findings refer specifically to Ruyan® ecigarettes only.

http://www.healthnz.co.nz/RuyanCartridgeReport30-Oct-08.pdf

<u>Life Sci.</u> 1996;58(16):1339-46. Long-term effects of inhaled nicotine. Waldum HL1, Nilsen OG, Nilsen T, Rørvik H, Syversen V, Sanvik AK, Haugen OA, Torp SH, Brenna E.

#### **Abstract**

Tobacco smoking has been reported to be associated with increased risk of cardiovascular disease and cancer, particularly of the lungs. In spite of extensive research on the health effects of tobacco smoking, the substances in tobacco smoke exerting these negative health effects are not completely known. Nicotine is the substance giving the subjective pleasure of smoking as well as inducing addiction. For the first time we report the effect on the rat of long-term (two years) inhalation of nicotine. The rats breathed in a chamber with nicotine at a concentration giving twice the plasma concentration found in heavy smokers. Nicotine was given for 20 h a day, five days a week during a two-year period. We could not find any increase in mortality, in atherosclerosis or frequency of tumors in these rats compared with controls. Particularly, there was no microscopic or macroscopic lung tumors nor any increase in pulmonary neuroendocrine cells. Throughout the study, however, the body weight of the nicotine exposed rats was reduced as compared with controls. In conclusion, our study does not indicate any harmful effect of nicotine when given in its pure form by inhalation.

http://www.ncbi.nlm.nih.gov/pubmed/8614291